

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
8 March 2001 (08.03.2001)

PCT

(10) International Publication Number
WO 01/15676 A2

(51) International Patent Classification⁷: **A61K 31/00**

627 E. Osborne Road, North Vancouver, British Columbia
V7N 1M8 (CA).

(21) International Application Number: **PCT/IB00/01492**

(74) Agent: **MBM & CO.**; P.O. Box 809, Station B, Ottawa,
Ontario K1P 5P9 (CA).

(22) International Filing Date:
1 September 2000 (01.09.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/151,977 1 September 1999 (01.09.1999) US
09/526,193 15 March 2000 (15.03.2000) US
60/213,958 23 June 2000 (23.06.2000) US

(81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

(71) Applicants: **UNIVERSITY OF BRITISH COLUMBIA** [CA/CA]; 2329 West Mall, Vancouver, British Columbia V6T 1Z4 (CA). **XENON GENETICS, INC.** [CA/CA]; Suite 100, 2386 East Mall, Vancouver, British Columbia V6T 1Z3 (CA).

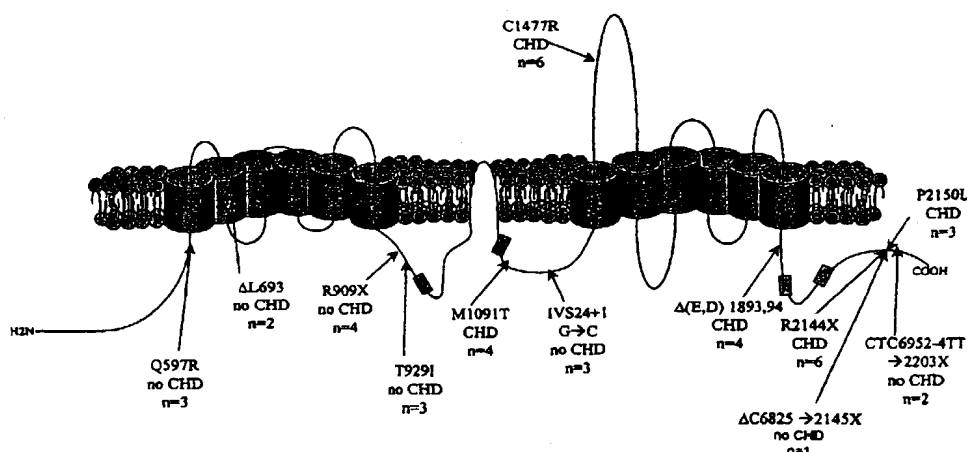
Published:

— Without international search report and to be republished upon receipt of that report.

(72) Inventors: **HAYDEN, Michael, R.**; 4484 West 7th Avenue, Vancouver, British Columbia V6R 1W9 (CA). **BROOKS-WILSON, Angela, R.**; 7100 Langton Road, Richmond, British Columbia V7C 4B2 (CA). **PIMSTONE, Simon, N.**; 4746 West 6th Avenue, Vancouver, British Columbia V6T 1C5 (CA). **CLEE, Susanne, M.**;

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: **COMPOSITIONS AND METHODS FOR MODULATING HDL CHOLESTEROL AND TRIGLYCERIDE LEVELS**



(57) Abstract: The invention features methods for treating patients having low HDL, a higher than normal triglyceride level, or a cardiovascular disease by administering compounds that modulate ABC1 expression or activity.

WO 01/15676 A2

COMPOSITIONS AND METHODS FOR MODULATING HDL
CHOLESTEROL AND TRIGLYCERIDE LEVELS

Background of the Invention

Low HDL cholesterol (HDL-C), or hypoalphalipoproteinemia, is a blood lipid abnormality which correlates with a high risk of cardiovascular disease (CVD), in particular coronary artery disease (CAD), but also cerebrovascular disease, coronary restenosis, and peripheral vascular disease. HDL-C levels are influenced by both environmental and genetic factors.

Epidemiological studies have consistently demonstrated that plasma HDL-C concentration is inversely related to the incidence of CAD. HDL-C levels are a strong graded and independent cardiovascular risk factor. Protective effects of an elevated HDL-C persist until 80 years of age. A low HDL-C is associated with an increased CAD risk even with normal (<5.2 mmol/l) total plasma cholesterol levels. Coronary disease risk is increased by 2% in men and 3% in women for every 1 mg/dL (0.026 mmol/l) reduction in HDL-C and in the majority of studies this relationship is statistically significant even after adjustment for other lipid and non-lipid risk factors. Decreased HDL-C levels are the most common lipoprotein abnormality seen in patients with premature CAD. Four percent of patients with premature CAD have an isolated form of decreased HDL-C levels with no other lipoprotein abnormalities while 25% have low HDL-C levels with accompanying hypertriglyceridemia.

Even in the face of other dyslipidemias or secondary factors, HDL-C levels are important predictors of CAD. In a cohort of diabetics, those with isolated low HDL-C had a 65% increased death rate compared to diabetics

with normal HDL-C levels (>0.9 mmol/l). Furthermore, it has been shown that even within high risk populations, such as those with familial hypercholesterolemia, HDL-C level is an important predictor of CAD. Low HDL-C levels thus constitute a major, independent, risk for CAD.

5 These findings have led to increased attention to HDL-C levels as a focus for treatment, following the recommendations of the National Cholesterol Education Program. These guidelines suggest that HDL-C values below 0.9 mmol/l confer a significant risk for men and women. As such, nearly half of patients with CAD would have low HDL-C. It is therefore
10 crucial that we obtain a better understanding of factors which contribute to this phenotype. In view of the fact that pharmacological intervention of low HDL-C levels has so far proven unsatisfactory, it is also important to understand the factors that regulate these levels in the circulation as this understanding may reveal new therapeutic targets.

15 Absolute levels of HDL-C may not always predict risk of CAD. In the case of CETP deficiency, individuals display an increased risk of developing CAD, despite increased HDL-C levels. What seems to be important in this case is the functional activity of the reverse cholesterol transport pathway, the process by which intracellular cholesterol is trafficked out of the cell to
20 acceptor proteins such as ApoAI or HDL. Other important genetic determinants of HDL-C levels, and its inverse relation with CAD, may reside in the processes leading to HDL formation and intracellular cholesterol trafficking and efflux. To date, this process is poorly understood, however, and clearly not all of the components of this pathway have been identified.
25 Thus, defects preventing proper HDL-mediated cholesterol efflux may be important predictors of CAD. Therefore it is critical to identify and understand novel genes involved in the intracellular cholesterol trafficking and efflux pathways.

HDL particles are central to the process of reverse cholesterol transport and thus to the maintenance of tissue cholesterol homeostasis. This process has multiple steps which include the binding of HDL to cell surface components, the acquisition of cholesterol by passive absorption, the esterification of this cholesterol by LCAT and the subsequent transfer of esterified cholesterol by CETP, to VLDL and chylomicron remnants for liver uptake. Each of these steps is known to impact the plasma concentration of HDL.

Changes in genes for ApoAI-CIII, lipoprotein lipase, CETP, hepatic lipase, and LCAT all contribute to determination of HDL-C levels in humans. One rare form of genetic HDL deficiency is Tangier disease (TD), diagnosed in approximately 40 patients world-wide, and associated with almost complete absence of HDL-C levels (listed in OMIM as an autosomal recessive trait (OMIM 205400)). These patients have very low HDL-C and ApoAI levels, which have been ascribed to impairment of lipid transport and hypercatabolism of nascent HDL and ApoAI, due to a delayed acquisition of lipid and resulting failure of conversion to mature HDL. TD patients accumulate cholesterol esters in several tissues, resulting in characteristic features, such as enlarged yellow tonsils, corneal opacity, hepatosplenomegaly, peripheral neuropathy, and cholesterol ester deposition in the rectal mucosa. Defective removal of cellular cholesterol and phospholipids by ApoAI as well as a marked deficiency in HDL mediated efflux of intracellular cholesterol has been demonstrated in TD fibroblasts. Even though this is a rare disorder, defining its molecular basis could identify pathways relevant for cholesterol regulation in the general population. The decreased availability of free cholesterol for efflux in the surface membranes of cells in Tangier Disease patients appears to be due to a defect in cellular lipid metabolism or trafficking. Approximately 45% of Tangier patients have signs of premature CAD, suggesting a strong link between decreased cholesterol efflux, low HDL-C and CAD. increased

As cholesterol is observed in the rectal mucosa of persons with TD, the molecular mechanism responsible for TD may also regulate cholesterol adsorption from the gastrointestinal (GI) tract.

5 A more common form of genetic HDL deficiency occurs in patients who have low plasma HDL-C usually below the 5th percentile for age and sex (OMIM 10768), but an absence of clinical manifestations specific to Tangier disease (Marcil *et al.*, *Arterioscler. Thromb. Vasc. Biol.* 19:159-169, 1999; Marcil *et al.*, *Arterioscler. Thromb. Vasc. Biol.* 15:1015-1024, 1995). These patients have no obvious environmental factors associated with this lipid
10 phenotype, and do not have severe hypertriglyceridemia nor have known causes of severe HDL deficiency (mutations in ApoAI, LCAT, or LPL deficiency) and are not diabetic. The pattern of inheritance of this condition is most consistent with a Mendelian dominant trait (OMIM 10768).

The development of drugs that regulate cholesterol metabolism has so
15 far progressed slowly. Thus, there is a need for a better understanding of the genetic components of the cholesterol efflux pathway. Newly-discovered components can then serve as targets for drugs.

Summary of the Invention

20 In a first aspect, the invention features a method for treating a patient diagnosed as having a lower than normal HDL-cholesterol level or a higher than normal triglyceride level. The method includes administering to the patient a compound that modulates LXR-mediated transcriptional activity. Preferably, the compound is administered to the patient with a
25 pharmaceutically acceptable carrier. The compound may be selected, for example, from the group consisting of 24-(S),25-epoxycholesterol; 24(S)-hydroxycholesterol; 22-(R)-hydroxycholesterol; 24(R),25-epoxycholesterol; 22(R)-hydroxy-24(S),25-epoxycholesterol; 22(S)-hydroxy-24(R),25-epoxycholesterol; 24-(S),25-iminocholesterol;

methyl-38-hydroxychololate; N,N-dimethyl-3 β -hydroxychololateamide;
24(R)-hydroxycholesterol; 22(S)-hydroxycholesterol;
22(R),24(S)-dihydroxycholesterol; 25-hydroxycholesterol;
22(R)-hydroxycholesterol; 22(S)-hydroxycholesterol;
5 24(S),25-dihydroxycholesterol; 24(R),25-dihydroxycholesterol;
24,25-dehydrocholesterol; 25-epoxy-22(R)-hydroxycholesterol;
20(S)-hydroxycholesterol; (20R,22R)-cholest-5-ene-3 β ,20,22-triol;
4,4-dimethyl-5- α -cholesta-8,14,24-trien-3- β -ol;
7 α -hydroxy-24(S),25-epoxycholesterol;
10 7 β -hydroxy-24(S),25-epoxycholesterol; 7-oxo-24(S),25-epoxycholesterol;
7 α -hydroxycholesterol; 7-oxocholesterol;
and desmosterol. In one preferred embodiment, the compound is an oxysterol.

In a second aspect, the invention features another method for treating a patient diagnosed as having a lower than normal HDL-cholesterol level or a higher than normal triglyceride level. This method includes administering to
15 the patient a compound that modulates RXR-mediated transcriptional activity. RXR-modulating compounds include hetero ethylene derivatives; tricyclic retinoids; trienoic retinoids; benzocycloalkenyl-alka:di- or trienoic acid derivatives; bicyclic-aromatic compounds and their derivatives;
20 bicyclicmethyl-aryl acid derivatives; phenyl-methyl heterocyclic compounds; tetrahydro-naphthyl compounds; arylthio-tetrahydro-naphthalene derivatives and heterocyclic analogues; 2,4-pentadienoic acid derivatives; tetralin-based compounds; nonatetraenoic acid derivatives; SR11237; dexamethasone; hydroxy, epoxy, and carboxy derivatives of methoprene; bicyclic benzyl,
25 pyridinyl, thiophene, furanyl, and pyrrole derivatives; benzofuran-acrylic acid derivatives; aryl-substituted and aryl and (3-oxo-1-propenyl)-substituted benzopyran, benzothiopyran, 1,2-dihydroquinoline, and 5,6-dihydronaphthalene derivatives; vitamin D3 (1,25-dihydroxyvitamin D3) and analogs; 24-hydroxylase inhibitor; mono-or polyenic carboxylic acid

derivatives ; tetrahydroquinolin-2-one-6 or 7-yl and related derivatives;
tetrahydronaphthalene; oxyiminoalkanoic acid derivatives; LG 100268; and
LGD 1069.

5 In a third aspect, the invention features a method for determining
whether a candidate compound modulates ABC1 expression by performing the
steps of: (a) providing a nucleic acid molecule that includes an ABC1
regulatory region or promoter operably linked to a reporter gene; (b) contacting
the nucleic acid molecule with the candidate compound; and (c) measuring
expression of the reporter gene, wherein altered reporter gene expression,
10 relative to a control not contacted with the compound, indicates that the
candidate compound modulates ABC1 expression. In various preferred
embodiments, the regulatory region includes 50 or more consecutive amino
acids selected from nucleotides 5854 to 6694, 7756 to 8318, 10479 to 10825,
15214 to 16068, 21636 to 22111, 27898 to 28721, 32951 to 33743, 36065 to
15 36847, 39730 to 40577, 4543 to 5287, or 45081 to 55639 of SEQ ID NO: 1.
In other preferred embodiments, the regulatory region 50 or more consecutive
amino acids selected from nucleotides 1 to 28,707 or 29,011 to 53,228 of SEQ
ID NO: 1. Preferably, the regulatory region includes a binding site for a
transcription factor selected from a group consisting of LXRs, RXRs, RORs,
20 SREBPs, and PPARs.

In a fourth aspect, the invention features a method for determining
whether a person has an altered risk for developing cardiovascular disease.
This method includes examining the person's ABC1 gene for polymorphisms
or mutations. The presence of a polymorphism or mutation associated with
25 cardiovascular disease indicates the person has an altered risk for developing
cardiovascular disease.

In a related aspect, the invention features a method for predicting a
person's response to a drug by determining whether the person has a
polymorphism in an ABC1 gene that alters the person's response to the drug.

Preferred polymorphisms are depicted in Fig. 4. In preferred embodiments of the fifth and sixth aspects, the polymorphism is in the 5' regulatory region of ABC1.

In a sixth aspect, the invention features a substantially purified LXR
5 response element comprising the nucleotide sequence
AGATCANNNNAGGTCA, wherein each N is, independently, C, T, G, or A
(SEQ ID NO: 231). Preferably, the LXR response element has the sequence
AGATCACTTGAGGTCA (SEQ ID NO: 232). Even more preferably, the
LXR response element consists essentially of the nucleotide sequence
10 AGATCANNNNAGGTCA, wherein each N is, independently, C, T, G, or A
(SEQ ID NO: 231).

In a seventh aspect, the invention features a substantially pure nucleic
acid molecule that consists essentially of a region that is substantially identical
to at least 50, 100, 150, 300, 500, 750, 1000, 2000, 3000, 4000, 5000 or all of
15 the consecutive nucleotides selected from nucleotides 5854 to 6694, 7756 to
8318, 10479 to 10825, 15214 to 16068, 21636 to 22111, 27898 to 28721,
32951 to 33743, 36065 to 36847, 39730 to 40577, 45081 to 55639, 4543 to
5287, 59188 to 60306, 60689 to 63548, 63574 to 65110, 65030 to 68312,
68605 to 73375, 73395 to 74692, 75586 to 77103, 74774 to 74920, 77519 to
20 87679, 87651 to 94160, 96916 to 97634, 94408 to 96595, 97807 to 98989,
100369 to 107171, 107179 to 107983, 108039 to 108998, 109222 to 118212,
118612 to 123911, 124586 to 138185, 137773 to 138393, 147497 to 148051,
158490 to 159118, 123718 to 125077, 137773 to 138912, , 139304 to 139699,
139351 to 146359, 146867 to 147637, 147733 to 149404, 149858 to 152699,
25 153064 to 153916, 153978 to 158516, 158719 to 160272, 160375 to 164458,
165279 to 169814, 164215 to 164592, 164786 to 165133, 165125 to 165429,
169882 to 170189, 170067 to 174018, 176845 to 178875, 179113 to 180606,
and 181723 to 183284 of SEQ ID NO: 1. In a related aspect, the invention
features a substantially pure nucleic acid molecule that has a region that is

substantially identical to nucleotides 5854 to 6694, 7756 to 8318, 10479 to 10825, 15214 to 16068, 21636 to 22111, 27898 to 28721, 32951 to 33743, 36065 to 36847, 39730 to 40577, 45081 to 55639, 4543 to 5287, 59188 to 60306, 60689 to 63548, 63574 to 65110, 65030 to 68312, 68605 to 73375, 73395 to 74692, 75586 to 77103, 74774 to 74920, 77519 to 87679, 87651 to 94160, 96916 to 97634, 94408 to 96595, 97807 to 98989, 100369 to 107171, 107179 to 107983, 108039 to 108998, 109222 to 118212, 118612 to 123911, 124586 to 138185, 137773 to 138393, 147497 to 148051, 158490 to 159118, 123718 to 125077, 137773 to 138912, , 139304 to 139699, 139351 to 146359, 146867 to 147637, 147733 to 149404, 149858 to 152699, 153064 to 153916, 153978 to 158516, 158719 to 160272, 160375 to 164458, 165279 to 169814, 164215 to 164592, 164786 to 165133, 165125 to 165429, 169882 to 170189, 170067 to 174018, 176845 to 178875, 179113 to 180606, or 181723 to 183284 of SEQ ID NO: 1. Preferred nucleic acid molecules have a region that is substantially identical or identical to nucleotides 1 to 28,707 of SEQ ID NO: 1 or nucleotides 29,011 to 53,228 of SEQ ID NO: 1.

In an eighth aspect, the invention features a method of treating a human having a lower than normal HDL-cholesterol level, a higher than normal triglyceride level, or a cardiovascular disease, including administering to the human an ABC1 polypeptide, or a cholesterol- or triglyceride-regulating fragment thereof, or a nucleic acid molecule encoding an ABC1 polypeptide, or a cholesterol- or triglyceride-regulating fragment thereof. In a preferred embodiment, the human has a low cholesterol or high triglyceride level relative to normal. Preferably, the ABC1 polypeptide is wild-type ABC1, or has a mutation that increases its stability or its biological activity. Preferably, the nucleic acid molecule is operably linked to a promoter and contained in an expression vector. Preferred mutations include the R \Rightarrow K mutation at position 219 and the V \Rightarrow A mutation at position 399 of ABC1. A preferred biological activity is improved regulation of cholesterol transport.

In a ninth aspect, the invention features a method of treating or preventing a lower than normal HDL-cholesterol level, a higher than normal triglyceride level, or a cardiovascular disease, including administering to an animal (e.g., a human) a compound that mimics the activity of wild-type ABC1, R219K ABC1, or V399A ABC1 or modulates the biological activity of ABC1.

One preferred cardiovascular disease that can be treated using the methods of the invention is coronary artery disease. Others include cerebrovascular disease and peripheral vascular disease.

The discovery that the ABC1 gene and protein are involved in cholesterol transport that affects serum HDL levels allows the ABC1 protein and gene to be used in a variety of diagnostic tests and assays for identification of HDL-increasing, triglyceride-lowering, or CVD-inhibiting drugs. In one family of such assays, the ability of domains of the ABC1 protein to bind ATP is utilized; compounds that enhance this binding are potential HDL-increasing or triglyceride-lowering drugs. Similarly, the anion transport capabilities and membrane pore-forming functions in cell membranes can be used for drug screening.

In a tenth aspect, ABC1 expression can also serve as a diagnostic tool for a lower than normal HDL-cholesterol level, a higher than normal triglyceride level, or CVD; determination of the genetic subtyping of the *ABC1* gene sequence can be used to subtype individuals or families with lower than normal HDL levels or higher than normal triglyceride levels to determine whether the lower than normal HDL or higher than normal triglyceride phenotype is related to ABC1 function. This diagnostic process can lead to the tailoring of drug treatments according to patient genotype (referred to as pharmacogenomics), including prediction of the patient's response (e.g., increased or decreased efficacy or undesired side effects upon administration of a compound or drug).

Antibodies to an ABC1 polypeptide can be used both as therapeutics and diagnostics. Antibodies are produced by immunologically challenging a B-cell-containing biological system, e.g., an animal such as a mouse, with an ABC1 polypeptide to stimulate production of anti-ABC1 protein by the B-cells, followed by isolation of the antibody from the biological system. Such antibodies can be used to measure ABC1 polypeptide in a biological sample such as serum, by contacting the sample with the antibody and then measuring immune complexes as a measure of the ABC1 polypeptide in the sample. Antibodies to ABC1 can also be used as therapeutics for the modulation of ABC1 biological activity.

Thus, in an eleventh aspect, the invention features a purified antibody that specifically binds to ABC1. In one preferred embodiment, the antibody modulates cholesterol or triglyceride levels when administered to a mammal.

In a twelfth aspect, the invention features a method for determining whether candidate compound is useful for modulating cholesterol or triglyceride levels, the method including the steps of: (a) providing an ABC1 polypeptide; (b) contacting the polypeptide with the candidate compound; and (c) measuring binding of the ABC1 polypeptide, wherein binding of the ABC1 polypeptide indicates that the candidate compound is useful for modulating cholesterol or triglyceride levels.

In a thirteenth aspect, the invention features a method for determining whether a candidate compound is useful for the treatment of a lower than normal HDL-cholesterol level, a higher than normal triglyceride level, or a cardiovascular disease. The method includes (a) providing an ABC transporter (e.g., ABC1); (b) contacting the transporter with the candidate compound; and (c) measuring ABC transporter biological activity, wherein increased ABC transporter biological activity, relative to a transporter not contacted with the compound, indicates that the candidate compound is useful for the treatment of a lower than normal HDL-cholesterol level, a higher than normal triglyceride

level, or a cardiovascular disease. Preferably the ABC transporter is in a cell or a cell free assay system.

In a fourteenth aspect, the invention features a method for determining whether candidate compound is useful for modulating cholesterol or triglyceride levels. The method includes (a) providing a nucleic acid molecule comprising an ABC transporter promoter operably linked to a reporter gene; (b) contacting the nucleic acid molecule with the candidate compound; and (c) measuring expression of the reporter gene, wherein increased expression of the reporter gene, relative to a nucleic acid molecule not contacted with the compound, indicates that the candidate compound is useful for modulating cholesterol or triglyceride levels.

In a fifteenth aspect, the invention features a non-human mammal having a transgene comprising a nucleic acid molecule encoding a mutated ABC1 polypeptide. In one embodiment, the mutation is a dominant-negative mutation, such as the M \Rightarrow T mutation at position 1091 of ABC1.

In a sixteenth aspect, the invention features an expression vector, a cell, or a non-human mammal that includes an *ABC1* nucleic acid molecule of the present invention.

In a related aspect, the invention features a cell from a non-human mammal having a transgene that includes a nucleic acid molecule of the present invention.

In an eighteenth aspect, the invention features a method for determining whether a candidate compound decreases the inhibition of a dominant-negative ABC1 polypeptide. The method includes (a) providing a cell expressing a dominant-negative ABC1 polypeptide; (b) contacting the cell with the candidate compound; and (c) measuring ABC1 biological activity of the cell, wherein an increase in the ABC1 biological activity, relative to a cell not contacted with the compound, indicates that the candidate compound decreases the inhibition of a dominant-negative ABC1 polypeptide. A preferred

dominant-negative ABC1 polypeptide is M1091T ABC1.

In a nineteenth aspect, the invention features a method of determining in a subject a propensity for a disease or condition selected from the group consisting of a lower than normal HDL level, a higher than normal triglyceride level, and a cardiovascular disease. This method involves determining the presence or absence of at least one ABC1 polymorphism in the polynucleotide sequence of an ABC1 regulatory region, promoter, or coding sequence or in the amino acid sequence of an ABC1 protein in a sample obtained from the subject, wherein the presence or absence of the ABC1 polymorphism is indicative of a risk for the disease or condition. Preferably, the method also includes analyzing at least five ABC1 polymorphic sites in the polynucleotide sequence or the amino acid sequence.

In a twentieth aspect, the invention features a method for determining whether an ABC1 polymorphism is indicative of a risk in a subject for a disease or condition selected from the group consisting of a lower than normal HDL level, a higher than normal triglyceride level, and a cardiovascular disease. The method includes (a) determining whether the prevalence of the disease or condition in a first subject or set of subjects differs from the prevalence of the disease or condition in a second subject or set of subjects; (b) analyzing the polynucleotide sequence of an ABC1 regulatory region, promoter, or coding sequence or the amino acid sequence of an ABC1 protein in a sample obtained from the first subject or set of subjects and the second subject or set of subjects; and

(c) determining whether at least one ABC1 polymorphism differs between the first subject or set of subjects and the second subject or set of subjects, wherein the presence or absence of the ABC1 polymorphism is correlated with the prevalence of the disease or condition, thereby determining whether the ABC1 polymorphism is indicative of the risk. Preferably, the method further includes analyzing at least five ABC1 polymorphic sites in the polynucleotide sequence

of an ABC1 regulatory region, promoter, or coding sequence or in the amino acid sequence of ABC1.

In a twenty-first aspect, the invention provides an electronic database having a plurality of sequence records of ABC1 polymorphisms correlated to
5 records of predisposition to or prevalence of a disease or condition selected from the group consisting of a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease.

In a twenty-second aspect, the invention features a method for selecting a preferred therapy for modulating ABC1 activity or expression in a subject.
10 This method includes (a) determining the presence or absence of at least one ABC1 polymorphism in the polynucleotide sequence of an ABC1 regulatory region, promoter, or coding sequence or in the amino acid sequence of an ABC1 protein in a sample obtained from the subject, wherein the presence or absence of the ABC1 polymorphism is indicative of the safety or efficacy of at
15 least one therapy for modulating ABC1 expression or activity; and (b) determining a preferred therapy for modulating ABC1 expression or activity in the subject. Preferably, the method further includes analyzing at least five ABC1 polymorphic sites in the polynucleotide sequence of an ABC1 regulatory region, promoter, or coding sequence or the amino acids sequence
20 of ABC1.

In a twenty-third aspect, the invention provides a method for determining whether a candidate compound is useful for the treatment of a disease or condition selected from the group consisting of a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a
25 cardiovascular disease. This method includes (a) providing an assay system having a measurable ABC1 biological activity; (b) contacting the assay system with the candidate compound; and (c) measuring ABC1 biological activity or ABC1 phosphorylation. Modulation of ABC1 biological activity or ABC1 phosphorylation in this assay system, relative to the ABC1 biological activity

or ABC1 phosphorylation in a corresponding control assay system not contacted with the candidate compound, indicates that the candidate compound is useful for the treatment of the disease or condition. In preferred embodiments, the assay system is a cell based system or a cell free system.

5 Preferably, the candidate compound modulates both ABC1 protein phosphorylation and ABC1 activity.

In a twenty-fourth aspect, the invention provides a method for identifying a compound to be tested for an ability to ameliorate a disease or condition selected from the group consisting of a lower than normal HDL
10 cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease. This method includes

(a) contacting a subject or cell with a candidate compound; (b) measuring ABC1 expression, activity, or protein phosphorylation in the subject or cell. Altered ABC1 expression, activity, or protein phosphorylation in this subject
15 or cell; relative to the ABC1 expression, activity, or protein phosphorylation in a corresponding control subject or cell not contacted with the candidate compound; identifies the candidate compound as a compound to be tested for an ability to ameliorate the disease or condition. Preferably, the candidate compound modulates both ABC1 protein phosphorylation and the ABC1
20 activity.

In a twenty-fifth aspect, the invention provides a method for determining whether a candidate compound is useful for modulating a disease or condition selected from the group consisting of a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular
25 disease. The method includes (a) providing a cell expressing an ABC1 gene or a fragment thereof;

(b) contacting the cell with the candidate compound; and (c) measuring ABC1 activity of the cell. Altered ABC1 activity in this cell, relative to the ABC1 activity in a corresponding control cell not contacted with the compound,

indicates that the candidate compound is useful for modulating the disease or condition.

In a twenty-six aspect, the invention provides a method for determining whether a candidate compound is useful for modulating a disease or condition selected from the group consisting of a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease. This method includes (a) contacting a cell expressing an ABC1 protein with the candidate compound; and (b) measuring the phosphorylation of the ABC1 protein. Altered ABC1 protein phosphorylation in this cell, relative to the ABC1 protein phosphorylation in a corresponding control cell not contacted with the candidate compound, indicates that the is useful for modulating the disease or condition.

In a twenty-seventh aspect, the invention provides a compound useful for the treatment of a disease or condition selected from the group consisting of a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease. The compound modulates ABC1 biological activity, and is identified by the steps of (a) providing an assay system having a measurable ABC1 biological activity; (b) contacting the assay system with the compound; and (c) measuring ABC1 biological activity, wherein modulation of ABC1 biological activity, relative to the ABC1 biological activity in a corresponding control assay system not contacted with the compound, indicates that the compound is useful for the treatment of the disease or condition.

In a twenty-eighth aspect, the invention provides a compound useful for the treatment of a disease or condition selected from the group consisting of a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease. The compound induces a change in ABC1 biological activity that mimics the change in ABC1 biological activity induced by the R219K ABC1 mutation.

In a twenty-ninth aspect, the invention provides a compound useful for the treatment of a disease or condition selected from the group consisting of a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease. The compound binds or interacts with
5 residue R219 of ABC1, thereby mimicking the change in ABC1 activity induced by the R219K ABC1 mutation.

In a thirtieth aspect, the invention provides a compound useful for the treatment of a disease or condition selected from the group consisting of a lower than normal HDL cholesterol level, a higher than normal triglyceride
10 level, and a cardiovascular disease. The compound induces a change in ABC1 biological activity that mimics the change in ABC1 biological activity induced by the V339A ABC1 mutation.

In a thirty-first aspect, the invention provides a compound useful for the treatment of a disease or condition selected from the group consisting of a
15 lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease. The compound binds or interacts with residue V399 of ABC1, thereby mimicking the change in ABC1 activity induced by the V399A ABC1 mutation.

In a thirty-second aspect, the invention provides a compound that
20 modulates ABC1 activity and binds or interacts with an amino acid of ABC1, wherein the amino acid is a residue selected from amino acids 119 to 319 of ABC1 (SEQ ID NO: 5) or amino acids 299 to 499 of ABC1 (SEQ ID NO: 5).

In a thirty-second aspect, the invention provides a method for determining whether a candidate compound is useful for the treatment a
25 disease or condition selected from the group consisting of a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease. This method involves (a) providing an assay system having a measurable LXR biological activity; (b) contacting the assay system with the candidate compound; and

(c) measuring LXR biological activity, wherein modulation of LXR biological activity, relative to the LXR biological activity in a corresponding control assay system not contacted with the candidate compound, indicates that the candidate compound is useful for the treatment of the disease or condition.

5 In a thirty-third aspect, the invention provides method for determining whether a candidate compound is useful for modulating ABC1 biological activity. This method involves (a) providing an assay system having a measurable LXR biological activity; (b) contacting the assay system with the candidate compound; and (c) measuring LXR biological activity, wherein
10 modulation of LXR biological activity, relative to the LXR biological activity in a corresponding control assay system not contacted with the candidate compound, indicates that the candidate compound is useful for modulating ABC1 biological activity. Preferably, the LXR biological activity is modulation of ABC1 expression.

15 In a thirty-fourth aspect, the invention provides method for identifying a compound to be tested for an ability to modulate ABC1 biological activity. This method involves (a) contacting a subject or cell with a candidate compound;
 (b) assaying the activity of the LXR gene product in the subject or cell;
20 wherein modulation of the activity, relative to the activity in a corresponding control subject or cell not contacted with the candidate compound, identifies the candidate compound as a compound to be tested for an ability to modulate the biological activity of ABC1.

 In a thirty-fifth aspect, the invention provides the use of an LXR gene
25 product in an assay to identify compounds useful for the treatment of a disease or condition selected from the group consisting of a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease.

In a thirty-sixth aspect, the invention features the use of a compound that modulates the activity or expression of an LXR gene product for the treatment of a disease or condition selected from the group consisting of a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease.

In a thirty-seventh aspect, the invention provides a method for identifying a compound to be tested for an ability to treat a disease or condition selected from the group consisting of a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease.

This method involves

(a) providing an assay system having a measurable LXR biological activity; (b) contacting the assay system with the candidate compound; and (c) measuring LXR biological activity, wherein modulation of the LXR biological activity, relative to the LXR biological activity in a corresponding control assay system not contacted with the candidate compound, identifies the candidate compound as a compound to be tested for an ability to treat the disease or condition.

In a thirty-eight aspect, the invention provides a method for screening an candidate LXR agonist for the ability to treat a disease or condition selected from the group consisting of a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease. This method involves

(a) contacting the a with the candidate LXR agonist; and (b) measuring cholesterol efflux activity of the cell, wherein an increase in the cholesterol efflux activity in the cell, relative to the cholesterol efflux in a corresponding control cell not contacted with the candidate LXR agonist, indicates that the candidate LXR agonist is useful for treating the disease or condition.

In a thirty-ninth aspect, the invention provides a method for screening a candidate LXR modulating compound for the ability to treat a disease or condition selected from the group consisting of a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease. This method involves (a) contacting a cell with the candidate LXR modulating compound; and
5 (b) measuring ABC1 biological activity of the cell; wherein an increase in ABC1 biological activity in the cell, relative to the ABC1 biological activity in a corresponding control cell not contacted with the LXR modulating
10 compound, indicates that the LXR modulating compound is useful for treating the disease or condition.

In another aspect, the invention provides a method for determining whether a candidate compound is useful for modulating triglyceride levels. The method involves (a) providing a cell comprising an ABC1 polypeptide
15 comprising amino acids 1 to 60 of SEQ ID NO: 5; (b) contacting the cell with the candidate compound; and (c) measuring the half-life of the ABC1 polypeptide,
wherein an increase in said half-life, relative to the half-life in a corresponding control cell not contacted with the compound, indicates that the candidate
20 compound is useful for modulating triglyceride levels.

In a related aspect, the invention features method for determining whether a candidate compound mimics ABC1 biological activity. The method includes (a) providing a cell that is not expressing an ABC1 polypeptide; (b)
contacting the cell with the candidate compound; and (c) measuring ABC1
25 biological activity of the cell, wherein altered ABC1 biological activity, relative to a corresponding control cell not contacted with the compound, indicates that the candidate compound modulates ABC1 biological activity. Preferably, the cell has an *ABC1* null mutation. In one preferred embodiment, the cell is in a mouse or a chicken (e.g., a WHAM chicken) in which its *ABC1*

gene has been mutated.

In a preferred embodiment of the screening methods of the present invention, the cell is in an animal. The preferred biological activity is transport of cholesterol (e.g., HDL cholesterol or LDL cholesterol) or interleukin-1, or is binding or hydrolysis of ATP by the ABC1 polypeptide. Preferably, the ABC1 polypeptide used in the screening methods includes amino acids 1-60 of SEQ ID NO: 5. Alternatively, the ABC1 polypeptide can include a region encoded by a nucleotide sequence that hybridizes under high stringency conditions to nucleotides 75 to 254 of SEQ ID NO: 6. Preferably, the subject is a human. Preferably, the cell or assay system has an exogenously supplied copy of an LXRE selected from the group consisting of SEQ ID NO: 94, SEQ ID NO: 92, and the LXRE consensus motif at nucleotide -7670 of the 3' end of intron 1. For various methods of the invention, a preferred LXR biological activity is modulation of ABC1 expression. A preferred LXR gene product is an ABC1 nucleic acid molecule or protein.

It is also contemplated that additional sequence of the ABC1 regulatory regions may be determined by sequencing the rest of the 4I8, 31J20, 47O19, or 179G21 Research Genetics RPCI-11 BACs using the methods described herein. Substantially pure nucleic acids containing regions substantially identical to at least 50, 100, 150, 300, 500, 750, 1000, 2000, 3000, 4000, 5000 consecutive nucleotides of these regions may be used in the methods of the present invention.

By "polypeptide" is meant any chain of more than two amino acids, regardless of post-translational modification such as glycosylation or phosphorylation.

By "reporter gene" is meant any gene which encodes a product whose expression is detectable and/or quantifiable by physical, immunological, chemical, biochemical, or biological assays. A reporter gene product may, for example, have one of the following attributes, without restriction: a specific

nucleic acid/chip hybridization pattern, fluorescence (e.g., green fluorescent protein), enzymatic activity (e.g., lacZ/ β -galactosidase, luciferase, chloramphenicol acetyltransferase), toxicity (e.g., ricin A), or an ability to be specifically bound by a second molecule (e.g., biotin or a detectably labeled antibody). It is understood that any engineered variants of reporter genes, which are readily available to one skilled in the art, are also included, without restriction, in the foregoing definition.

By "operably linked" is meant that a gene and a regulatory sequence are connected in such a way as to permit expression of the gene product under the control of the regulatory sequence. A promoter may also be operably linked to a gene such that expression of the gene product is under control of the promoter.

By "regulatory region" is meant a region that, when operably linked to a promoter and a gene (e.g., a reporter gene), is capable of modulating the expression of the gene from the promoter. Regulatory regions include, for example, nuclear hormone transcription factor binding sites such as those described herein and may be found in intronic sequence.

By "promoter" is meant a minimal sequence sufficient to direct transcription of an operably-linked gene.

By "substantially identical" is meant a polypeptide or nucleic acid exhibiting at least 50%, preferably 85%, more preferably 90%, and most preferably 95% identity to a reference amino acid or nucleic acid sequence. For polypeptides, the length of comparison sequences will generally be at least 16 amino acids, preferably at least 20 amino acids, more preferably at least 25 amino acids, and most preferably 35 amino acids. For nucleic acids, the length of comparison sequences will generally be at least 50 nucleotides, preferably at least 60 nucleotides, more preferably at least 75 nucleotides, and most preferably 110 nucleotides. One sequence may include additions or deletions (i.e., gaps) of 20% or less when compared to the second sequence.

Optimal alignment of sequences may be conducted, for example, by the methods of Gish and States (Nature Genet. 3:266-272, 1993), Altshul *et al.* (J. Mol. Biol. 215:403-410, 1990), Madden *et al.* (Meth. Enzymol. 266:131-141, 1996), Althsul *et al.* (Nucleic Acids Res. 25:3389-3402, 1997), or Zhang *et al.* (Genome Res. 7:649-656, 1997).

Sequence identity is typically measured using sequence analysis software with the default parameters specified therein (e.g., Sequence Analysis Software Package of the Genetics Computer Group, University of Wisconsin Biotechnology Center, 1710 University Avenue, Madison, WI 53705). This software program matches similar sequences by assigning degrees of homology to various substitutions, deletions, and other modifications. Conservative substitutions typically include substitutions within the following groups: glycine, alanine, valine, isoleucine, leucine; aspartic acid, glutamic acid, asparagine, glutamine; serine, threonine; lysine, arginine; and phenylalanine, tyrosine.

By "substantially pure nucleic acid" is meant nucleic acid that is free of the genes which, in the naturally-occurring genome of the organism from which the nucleic acid of the invention is derived, flank the nucleic acid. The term therefore includes, for example, a recombinant nucleic acid that is incorporated into a vector; into an autonomously replicating plasmid or virus; into the genomic nucleic acid of a prokaryote or a eukaryote cell; or that exists as a separate molecule (e.g., a cDNA or a genomic or cDNA fragment produced by PCR or restriction endonuclease digestion) independent of other sequences. It also includes a recombinant nucleic acid that is part of a hybrid gene encoding additional polypeptide sequence.

By "high stringency conditions" is meant hybridization in 2X SSC at 40°C with a DNA probe length of at least 40 nucleotides. For other definitions of high stringency conditions, see F. Ausubel *et al.*, *Current Protocols in Molecular Biology*, pp. 6.3.1-6.3.6, John Wiley & Sons, New

York, NY, 1994, hereby incorporated by reference.

By "modulates" is meant increase or decrease. Preferably, a compound that modulates LXR-mediated transcription, RXR-mediated transcription, ABC1 gene expression, HDL-C levels, or triglyceride levels does so by at least 5%, more preferably by at least 10%, and most preferably by at least 25% or even at least 50%.

By "purified antibody" is meant antibody which is at least 60%, by weight, free from proteins and naturally occurring organic molecules with which it is naturally associated. Preferably, the preparation is at least 75%, more preferably 90%, and most preferably at least 99%, by weight, antibody. A purified antibody may be obtained, for example, by affinity chromatography using recombinantly-produced protein or conserved motif peptides and standard techniques.

By "specifically binds" is meant an antibody that recognizes and binds to, for example, a human ABC1 polypeptide but does not substantially recognize and bind to other non-ABC1 molecules in a sample, e.g., a biological sample, that naturally includes protein. A preferred antibody binds to the ABC1 polypeptide sequence of Fig. 2A (SEQ ID NO: 5).

By "polymorphism" is meant that a nucleotide or nucleotide region is characterized as occurring in several different forms. A "mutation" is a form of a polymorphism in which the expression level, stability, function, or biological activity of the encoded protein is substantially altered.

By "LXR" is meant nuclear receptors LXR α and LXR β . Preferred LXRs include human LXR α (GenBank accession no. Q13133) and human LXR β (GenBank accession no. P55055)(see Apfel *et al.*, Mol. Cell. Biol. 14:7025-7035, 1994; Willy *et al.*, Genes Dev. 9:1033-1045, 1995; and Song *et al.*, Proc. Natl. Acad. Sci. USA 91:10809-10813, 1995, each of which is hereby incorporated by reference).

By "RXR" is meant nuclear receptors RXR α , RXR β , and RXR γ . Preferred RXRs include human RXR α (GenBank accession no. Q13133), human RXR β (GenBank accession no. S37781), and human RXR γ (GenBank accession no. Q13133).

5 By "ABC transporter" or "ABC polypeptide" is meant any transporter that hydrolyzes ATP and transports a substance across a membrane. Preferably, an ABC transporter polypeptide includes an ATP Binding Cassette and a transmembrane region. Examples of ABC transporters include, but are not limited to, ABC1, ABC2, ABCR, and ABC8.

10 By "ABC1 polypeptide" is meant a polypeptide having substantial identity to an ABC1 polypeptide having the amino acid sequence of SEQ ID NO: 5.

By "ABC biological activity" or "ABC1 biological activity" is meant hydrolysis or binding of ATP, transport of a compound (e.g., cholesterol, interleukin-1) or ion across a membrane, or regulation of cholesterol or phospholipid levels (e.g., either by increasing or decreasing HDL-cholesterol or LDL-cholesterol levels).

15 The invention provides methods for treating patients having low HDL-C and/or higher than normal triglyceride levels by administering compounds that modulate ABC1 biological activity or expression. For example, the compounds may modulate the transcriptional activity of LXR/RXR heterodimers. Many compounds that modulate LXR transcriptional activity or RXR transcriptional activity are known in the art. Preferred compounds of the invention are oxysterols; additional compounds are described herein.

25 The invention also provides screening procedures for identifying therapeutic compounds (cholesterol-modulating, triglyceride-modulating, or anti-CVD pharmaceuticals) which can be used in human patients. Compounds that modulate ABC1 biological activity or expression are considered useful in the invention, as are compounds that modulate ABC concentration, protein

stability, regulated catabolism, or its ability to bind other proteins or factors. In general, the screening methods of the invention involve screening any number of compounds for therapeutically active agents by employing any number of *in vitro* or *in vivo* experimental systems. Exemplary methods useful for the identification of such compounds are detailed below.

The methods of the invention simplify the evaluation, identification and development of active agents for the treatment and prevention of low HDL, higher than normal triglyceride levels, and CVD. In general, the screening methods provide a facile means for selecting natural product extracts or compounds of interest from a large population which are further evaluated and condensed to a few active and selective materials. Constituents of this pool are then purified and evaluated in the methods of the invention to determine their HDL-raising, triglyceride-lowering, anti-CVD activities, or a combination thereof.

Other features and advantages of the invention will be apparent from the following description of the preferred embodiments thereof.

Brief Description of the Drawings

Fig. 1 shows the genomic sequence of human ABC1, including exons 1-50 (SEQ ID NO: 1). Capital letters denote exonic sequence, lower case letters denote 5' regulatory sequence or intronic sequence. "Z" denotes any nucleotide or other, including no nucleotide. The numbering used herein for the nucleotides in SEQ ID No:1 assumes that no nucleotide is present at the positions denoted "z;" however, it would be readily apparent to one skilled in the art that the numbering of the nucleotides in these sequences would change if a nucleotide is present at some or all of the positions denoted "z." "K" denotes nucleotides G or T; "Y" denotes nucleotides C or T; "R" denotes nucleotides A or G; "M" denotes nucleotides A or C; "S" denotes nucleotides C or G; "H" denotes nucleotides A, C, or T; "B" denotes nucleotides C, G, or

T. Because of the identification of an ABC1 exon upstream of exon 0 that we previously disclosed, the numbering used herein to refer to ABC1 exons has been increased by one compared to our previously used numbering (U.S.S.N. 09/526,193; U.S.S.N. 60/124,702; U.S.S.N. 60/138,048; U.S.S.N. 60/139,600; 5 U.S.S.N. 60/151,977). For example, the previously described exon 0 is referred to herein as exon 1.

Fig. 2A is the amino acid sequence of the human ABC1 protein (SEQ ID NO: 5). Fig. 2B is the nucleotide sequence of the human ABC1 cDNA (SEQ ID NO: 6).

10 Fig. 3 is a summary of locations of consensus transcription factor binding sites in the human ABC1 5' regulatory sequence. The abbreviations are as follows: PPRE=peroxisome proliferator-activated receptor. SREBP=steroid response element-binding protein site. ROR=RAR-related orphan receptor. The numbering used herein for the locations of the 15 transcription factor binding sites assumes that no nucleotide is present at the positions denoted "z" in SEQ ID NO: 1. For the polymorphisms in the promoter region, the numbering is based on the first base of the promoter as nucleotide number -1. For exon 1, the numbering is based on the first base of exon 1 as nucleotide number +1. 20 For the 5' end intron 1, the numbering is based on the first position in intron 1 as +1. For the 3' end of intron 1, the numbering is based on the first base '5 to the start of exon 2 as nucleotide number -1.

Fig. 4 is a table summarizing polymorphisms in the genomic ABC1 sequences.

25 Figs. 5A and 5B are bar graphs showing the percent of heterozygotes or unaffected family members with HDL (Fig. 5A) and triglycerides (TG) (Fig 5B) within a given range of percentiles for age and sex, based on the LRC criteria (Heiss *et al.*, Circulation 62:IV-116-IV-136, 1980). A broad distribution of HDL levels was seen in the heterozygotes, extending up to the

31st percentile for age and sex. Although there is overlap in the distribution of triglycerides between heterozygotes and unaffected family members, a larger portion of heterozygotes have triglyceride levels greater than the 80th percentile for age and sex.

5 Fig. 6 is a table characterizing TD patients, ABC1 heterozygotes, and unaffected family members.

 Fig. 7 is a table summarizing the incidence of CAD in ABC1 heterozygotes.

 Fig. 8 is a graph showing the average HDL levels in heterozygotes for each mutation versus the efflux levels measured in a heterozygous carrier of each mutation. The HDL levels are expressed as the percentage of the mean HDL level in the unaffected members of that family. The efflux levels are highly correlated with the levels of HDL cholesterol and are associated with 82% of the variation in HDL cholesterol levels.

15 Fig. 9 is a table summarizing the HDL levels and presence or absence of CAD in ABC1 heterozygotes. In the R2144X and R909X ABC1 mutations, the codon encoding Arg2133 or Arg909 is mutated to a STOP codon resulting in truncation of the encoded protein. In the "Del E,D 1893,94" mutation, the codons encoding Glu1893 and Asp1894 are deleted. The "invs25 + 1G-->C" mutation converts the first nucleotide of intron 25 from a "G" to a "C," removing a splice site. For the "del C6825-->2145X" mutation, the deletion of C6825 in the nucleotide sequence is a frame-shift mutation that results in a STOP codon at the codon corresponding to amino acid 2145 of the encoded protein. For the "CTC6952-4TT-->2203X" mutation, "CTC" is replaced by

20 "TT" in the nucleotide sequence, resulting in the conversion of the codon encoding amino acid 2203 to a stop codon.

 Fig. 10 is a table comparing the mean lipid levels in unaffected family members and ABC1 heterozygotes with either missense or sever mutations.

Fig. 11 is a schematic diagram of the ABC1 protein, illustrating the location of the mutations and the presence or absence of CAD in carriers of the mutations. The number (n) of heterozygotes who are 40 years or older and may have developed CAD are listed.

5 Figs. 12A and 12B are pedigrees of two FHA kindreds, FHA3 and FHA1, respectively (Marcil *et al.*, Lancet 354:1341-1346, 1999). Males are denoted by square symbols, females by circles. Individuals heterozygous for mutations are given half-shaded symbols, with the probands indicated by arrows. A diagonal line indicates a deceased individual. The youngest
10 individuals have HDL cholesterol at higher percentile ranges than those in the older generations.

Fig. 13 is a bar graph showing the percentage of individuals less than 30 years of age and from 30 to less than 70 years of age with HDL cholesterol levels in a given percentile range. Younger individuals have a far broader
15 distribution of HDL cholesterol levels, clearly indicating that the impact of ABC1 on HDL levels is influenced by age.

Fig. 14 is a table summarizing HDL and TG levels in different age groups for ABC1 heterozygotes and unaffected family members.

Figs. 15A and 15B are graphs showing the mean HDL level in
20 heterozygous males (Fig. 15A) and females (Fig. 15B) in 10 year age groups (plotted at the half-way point) compared to the 10th percentile distribution in the LRC population (Heiss *et al.*, *supra*). Error bars represent the standard deviation of each mean. The number of individuals in each group is shown under each data point. Beyond the age of 30, mean HDL levels in
25 heterozygotes fall much lower than the 10th percentile distribution; in contrast, mean HDL cholesterol levels in the heterozygotes less than 30 years old more closely approximate the 10th percentile distribution.

Figs. 16A and 16B are graphs showing the mean HDL (Fig. 16A) and triglyceride levels (Fig. 16B) in heterozygotes and unaffected family members falling within each tertile of BMI. The tertiles of BMI correspond to the following values: (1) BMI <21.4; (2) 21.4<BMI<25.1; (3) BMI>25.1.

5 Fig. 17 is a table showing the oligonucleotides and reaction conditions used for RFLP screening of ABC1 polymorphisms.

Fig. 18 is a picture of a gel showing RFLP genotyping of the R219K variant. The 177 base pair PCR product is not digested for the A allele, whereas the B allele is digested producing fragments of 107 and 70 base pairs.

10 Fig. 19 is a table showing the allele frequencies of polymorphisms in the ABC1 gene.

Fig. 20 is a table comparing MSD, MOD, and frequency of coronary events in R219K ABC1 variant carriers compared to controls.

15 Fig. 21 is a graph showing the event-free survival curves for carriers (AB+BB) and non-carriers (AA) of the R219K ABC1 variant. Carriers of the variant have a 29% increased event-free survival over the two years of the trial, compared with non-carriers.

20 Fig. 22 is a table showing the baseline demographics and lipid levels in the Regression Growth Evaluation Statin Study (REGRESS) cohort by R219K ABC1 genotype.

Fig. 23 is a table showing the lipid levels and CAD above and below the median age in R219K ABC1 carriers and controls.

25 Fig. 24 is a bar graph showing the percent difference in HDL cholesterol levels between those greater and less than the median age (56.7 years) for each R219K genotype.

Figs. 25A and 25B are graphs showing the correlations of HDL cholesterol (Fig. 25A) and efflux (Fig. 25B) with age, by R219K genotype.

Figs. 26A and 26B are graphs showing the change in MSD (Fig. 26A) and MOD (Fig. 26B) by median age in carriers (AB+BB) and non-carriers (AA) of the R219K ABC1 variant.

Fig. 27 is a table showing the ethnic distribution of the R219K ABC1 variant.

Detailed Description

We have previously discovered that the human ABC1 (also known as ABCA1) genomic region contains consensus binding sites for transcription factors such as LXRs, RXRs, PPARs, SREBPs, and RORs. In the present invention, we report the sequence of additional regions of the ABC1 regulatory region which also contain consensus binding sites for transcription factors. We also discovered that heterozygotes for ABC1 mutations have age-modulated decreases in HDL, increases in triglyceride levels, and significantly increased risk for CAD. Furthermore, this phenotype was highly correlated with efflux, clearly demonstrating that impairment of reverse cholesterol transport is associated with decreased plasma HDL cholesterol, increased triglyceride levels, and increased atherogenesis. Accordingly, the present invention features screening methods to identify therapies that increase ABC1 function, resulting in increased plasma HDL cholesterol, decreased triglyceride levels, protection against atherosclerosis, or a combination of these effects.

Genes play a significant role influencing HDL levels. Tangier disease (TD) was the first reported genetic HDL deficiency. Until recently, the molecular basis for TD was unknown, but now mutations in ABC1 have been identified in TD patients (described below). For example, we have identified two additional probands and their families, and confirmed linkage and refined the locus to a limited genomic region. Mutations in the *ABC1* gene accounting for all four alleles in these two families were detected. A more frequent cause of low HDL levels is a distinct disorder, familial HDL deficiency (FHA). On

the basis of independent linkage, meiotic recombinants and disease associated haplotypes, FHA was localized to a small genomic region encompassing the *ABCI* gene. A mutation in a conserved residue in *ABCI* segregated with FHA. Antisense reduction of the *ABCI* transcript in fibroblasts was associated with a significant decrease in cholesterol efflux.

Cholesterol is normally assembled with intracellular lipids and secreted, but in TD the process is diverted and cholesterol is degraded in lysosomes. This disturbance in intracellular trafficking of cholesterol results in an increase in intracellular cholesterol ester accumulation associated with morphological changes of lysosomes and the Golgi apparatus and cholesteryl ester storage in histiocytes, Schwann cells, smooth muscle cells, mast cells and fibroblasts.

The clinical and biochemical heterogeneity in patients with TD has led to the possibility that genetic heterogeneity may also underlie this disorder. Considering this, we initially performed linkage analysis on these two families of different ancestries (TD-1 is Dutch, TD-2 is British; Frohlich *et al.*, Clin. Invest. Med. 10:377-382, 1987) and confirmed that the genetic mutations underlying TD in these families were localized to the same 9q31 region, to which a large family with TD had been assigned (Rust *et al.*, Nature Genetics 20:96-98, 1998). Detailed haplotype analysis, together with the construction of a physical map, refined the localization of this gene. Mutations in the *ABCI* gene were found in TD.

FHA is much more common than TD, although its precise frequency is not known. While TD has been described to date in only 40 families, we have identified more than 40 FHA families in the Netherlands and Quebec alone. After initial suggestions of linkage to 9q31, thirteen polymorphic markers spanning approximately 10 cM in this region were typed and demonstrated the highest LOD score at D9S277. Analysis of the homozygosity of markers in the TD-2 proband, who was expected to be homozygous for markers close to TD due to his parents' consanguinity, placed the TD gene distal to D9S127.

Combined genetic data from TD and FHA families pointed to the same genomic segment spanning approximately 1,000 kb between D9S127 and D9S1866. The *ABCI* transporter gene was contained within the minimal genomic region. RT-PCR analysis in one family demonstrated a deletion of leucine at residue 693 ($\Delta 693$) in the first transmembrane domain of ABC1, which segregated with the phenotype of HDL deficiency in this family.

ABC1 is part of the ATP-binding cassette (ABC transporter) superfamily, which is involved in energy-dependent transport of a wide variety of substrates across membranes (Dean *et al.*, Curr. Opin. Gen. Dev. 5:779-785, 1995). These proteins have characteristic motifs conserved throughout evolution which distinguish this class of proteins from other ATP binding proteins. In humans these genes essentially encode two ATP binding segments and two transmembrane domains (Dean *et al.*, Curr. Opin. Gen. Dev. 5:779-785, 1995). We have now shown that the ABC1 transporter is crucial for intracellular cholesterol transport.

We have demonstrated that reduction of the *ABCI* transcript using oligonucleotide antisense approaches results in decreased efflux, clearly demonstrating the link between alterations in this gene and its functional effects. TD and FHA now join the growing list of genetic diseases due to defects in the ABC group of proteins including cystic fibrosis (Zielenski, *et al.*, Annu. Rev. Genet. 29:777-807, 1995), adrenoleukodystrophy (Mosser *et al.*, Nature 361: 726-730, 1993), Zellweger syndrome (Gärtner *et al.*, Nat. Genet. 1:23, 1992), progressive familial intrahepatic cholestasis (Bull *et al.*, Nat. Genet. 18:219-224, 1998), and different eye disorders including Stargardt disease (Allikmets *et al.*, Nat. Genet. 15:236-246, 1997), autosomal recessive retinitis pigmentosa (Allikmets *et al.*, Science 277:1805-1807, 1997), and cone-rod dystrophy (Cremers *et al.*, Hum. Mol. Genet. 7:355-362, 1998).

Patients with TD have been distinguished from patients with FHA on the basis that Tangier disease was an autosomal recessive disorder (OMIM 20540) while FHA is inherited as an autosomal dominant trait (OMIM 10768). Furthermore, patients with TD have obvious evidence for intracellular
5 cholesterol accumulation which is not seen in FHA patients. It is now evident that heterozygotes for TD do have reduced HDL levels and that the same mechanisms underlie the HDL deficiency and cholesterol efflux defects seen in heterozygotes for TD as well as FHA. Furthermore, the more severe phenotype in TD represents loss of function from both alleles of the *ABC1*
10 gene.

ABC1 is activated by protein kinases, presumably via phosphorylation, which also provides one explanation for the essential role of activation of protein kinase C in promoting cholesterol efflux (Drobnick *et al.*, *Arterioscler. Thromb. Vasc. Biol.* 15: 1369-1377, 1995). Brefeldin, which inhibits
15 trafficking between the endoplasmic reticulum and the Golgi, significantly inhibits cholesterol efflux, essentially reproducing the effect of mutations in *ABC1*, presumably through the inhibition of *ABC1* biological activity. This finding has significance for the understanding of mechanisms leading to premature atherosclerosis. TD homozygotes develop premature coronary
20 artery disease, as seen in the proband of TD-1 (III-01) who had evidence for coronary artery disease at 38 years. This is particularly noteworthy as TD patients, in addition to exhibiting significantly reduced HDL, also have low LDL cholesterol, and yet they develop atherosclerosis despite this. This highlights the importance of HDL intracellular transport as an important
25 mechanism in atherogenesis. There is significant evidence that heterozygotes for TD are also at increased risk for premature vascular disease (Schaefer *et al.*, *Ann. Int. Med.* 93:261-266, 1980; Serfaty-Lacroisniere *et al.*, *Atherosclerosis* 107:85-98, 1994). There is also preliminary evidence for premature atherosclerosis in some probands with FHA (e.g., the proband in

FHA-2 (III-01) had a coronary artery bypass graft at 46 years while the proband in FHA-3 had evidence for CAD around 50 years of age. The TD-1 proband had more severe efflux deficiency than the TD-2 proband.

5 Interestingly, the TD-2 proband had no evidence for CAD by 62 when he died of unrelated causes, providing preliminary evidence for a relationship between the degree of cholesterol efflux (mediated in part by the nature of the mutation) and the likelihood of atherosclerosis.

The *ABCI* gene plays a crucial role in cholesterol transport and, in particular, intracellular cholesterol trafficking in monocytes and fibroblasts. It
10 also appears to play a significant role in other tissues such as the nervous system, GI tract, and the cornea. Completely defective intracellular cholesterol transport results in peripheral neuropathy, corneal opacities, and deposition of cholesterol esters in the rectal mucosa.

HDL deficiency is heterogeneous in nature. The delineation of the
15 genetic basis of TD and FHA underlies the importance of this particular pathway in intracellular cholesterol transport, and its role in the pathogenesis of atherosclerosis. Unraveling of the molecular basis for TD and FHA defines a key step in a poorly defined pathway of cholesterol efflux from cells and could lead to new approaches to treatment of patients with HDL deficiency in
20 the general population.

HDL has been implicated in numerous other biological processes, including but not limited to: prevention of lipoprotein oxidation; absorption of endotoxins; protection against *Trypanosoma brucei* infection; modulation of endothelial cells; and prevention of platelet aggregation (see Genest *et al.*, J.
25 Invest. Med. 47: 31-42, 1999, hereby incorporated by reference). Any compound that modulates HDL levels may be useful in modulating one or more of the foregoing processes. Our previous discovery that ABC1 functions to regulate HDL levels links, for the first time, ABC1 with the foregoing processes.

With the identification of the ABC1 protein as a key initiator of the efflux pathway, it has now been possible to directly examine the relationship between efflux, HDL, triglyceride level, and CAD. We have characterized the phenotypes of heterozygotes for several mutations in the ABC1 gene in a large cohort where diagnosis has been made by mutation identification.

Furthermore, the phenotype of the heterozygotes was compared to that of unaffected family members, enabling the results to be controlled, at least in part, for other genetic and environmental influences. In contrast, prior studies in obligate heterozygotes have been limited to small numbers, often within a single family, and thus restricted in the ability to analyze the phenotypic expression with multiple mutations over a range of ages.

A cohort of 77 individuals heterozygous for multiple mutations in the ABC1 gene were identified, enabling the characterization of 13 ABC1 mutations in 11 families (5 TD, 6 FHA). The ABC1 heterozygotes have an approximate 50% decrease in HDL cholesterol and apoAI, and a mild but significant decrease in apoAII. In addition, ABC1 heterozygotes have increased triglycerides, but in contrast to TD patients, have no significant change in total or LDL cholesterol. The changes in HDL, apoAI, and triglycerides were gene-dose dependent, suggesting that they are directly related to ABC1 function. Furthermore, heterozygotes have an over three-fold increased risk of developing CAD, and younger average age-of-onset compared to unaffected individuals. Further, the heterozygotes with the most severe deficiency in efflux had a higher frequency and greater severity of CAD. Interestingly, the severity of the phenotype observed in the heterozygotes appeared to be mutation-dependent, but there was no obvious relationship between the site of mutation and the phenotype. There was a trend toward lower HDL in carriers of severe mutations that caused truncations or null alleles than in carriers of missense mutations. One notable exception is the M1091T missense mutation which had the most severe phenotype, with

marked reductions in HDL cholesterol and efflux in affected family members, suggesting that this mutation may act in a dominant-negative fashion, down-regulating the function of the wild-type allele. Another interesting finding is the small cluster of mutations at the very C-terminal region of the protein, which suggests that this region is critical for ABC1 function.

The severe HDL deficiency in ABC1 heterozygotes suggests that residual cholesterol efflux is the major determinant of HDL cholesterol levels. Here we demonstrated a strong correlation between cholesterol efflux and HDL cholesterol levels. From the regression equation of mean HDL on efflux, each 8% increase in relative efflux is predicted to be associated with a 0.1 mmol/L increase in HDL cholesterol levels. For example, to effect a 30% increase in HDL cholesterol in a 40 year old male, it would require a 50% increase in ABC1 mediated cholesterol efflux. Although these numbers may not directly extrapolate to what is observed in a general population where other genetic and environmental factors have not been controlled for, these data nonetheless suggest that relatively small changes in ABC1 function may have a significant impact on plasma HDL cholesterol levels. Furthermore, the data presented here suggest that variations in efflux due to variations in ABC1 function directly reflect not only plasma HDL cholesterol levels but also triglyceride levels and CAD susceptibility, thus providing direct validation of the reverse cholesterol transport hypothesis and validation of ABC1 as a therapeutic target to raise HDL cholesterol, lower triglyceride levels, and protect against atherosclerosis.

The phenotype in ABC1 heterozygotes is also age-modulated. From 20 years of age in members of the control cohort, there is a small but definite increase in HDL with advancing age that is obviously absent in the heterozygotes. One explanation for this finding is that there is normally an age-related increase in ABC1 function, which is not seen in heterozygotes, perhaps because the remaining functioning allele has already been maximally

up-regulated secondary to an increase in intracellular cholesterol. This lack of age-related increase in ABC1 function in heterozygotes would exaggerate the difference in HDL levels between heterozygotes and control individuals in older age groups. There is some evidence for an age-modulated increase in expression of ABC transporters (Gupta, *Drugs Aging* 7:19-29, 1995). Further, evidence of a potential age-related increase in ABC1 function comes from the observation that the percentage of apoAI found in the pre β_1 subfraction of HDL, the predominant cholesterol acceptors, decreases with age, suggesting increased formation of mature α -migrating HDL with age.

In a Regression Growth Evaluation Statin Study, carriers of the R219K ABC1 mutation were found to have significantly lower triglyceride levels than individuals without this mutation. This result suggests that compounds that bind near Arg219 in wild-type ABC1 or otherwise mimic the function provided by Lys219 in the R219K ABC1 variant may lower triglyceride levels, and thus decrease risk of CAD. In addition, carriers of the V399A ABC1 variant had higher HDL levels and fewer coronary events than individuals without this variant. Thus, compounds that bind near Val399 in wild-type ABC1 or mimic the function provided by Ala399 in the V399A ABC1 variant may increase cholesterol levels and decrease risk of CAD. Determining the presence or absence of the R219K or V399A ABC1 variants in individuals may be useful in selecting therapies (such as HDL-lowering, triglyceride-raising, or anti-CAD therapies) for these subjects.

The following examples are to illustrate the invention. They are not meant to limit the invention in any way.

Analysis of TD Families

Studies of cholesterol efflux

Both probands had evidence of marked deficiency of cholesterol efflux similar to that previously demonstrated in TD patients. TD-1 is of Dutch

descent while TD-2 is of British descent.

Linkage analysis and establishment of a physical map

Multiple DNA markers were genotyped in the region of 9q31 to which
5 linkage to TD had been described (Rust *et al.*, Nat. Genet. 20, 96-98, 1998).

Two point linkage analysis gave a maximal peak LOD score of 6.49 at
D9S1832

with significant evidence of linkage to all markers in a ~10 cM interval.

Recombination with the most proximal marker, D9S1690 was seen in II-09 in
10 Family TD-1, providing a centromeric boundary for the disease gene.

Multipoint linkage analysis of these data did not increase the precision of the
positioning of the disease trait locus.

A physical map spanning approximately 10 cM in this region was
established with the development of a YAC contig. In addition, 22 other
15 polymorphic multi-allelic markers which spanned this particular region were
mapped to the contig, and a subset of these were used in construction of a
haplotype for further analysis.

While the family of Dutch decent did not demonstrate any
consanguinity, the proband in TD-2 was the offspring of a first-cousin
20 consanguineous marriage. We postulated, therefore, that it was most likely
that this proband would be homozygous for the mutation while the proband in
the Dutch family was likely to be a compound heterozygote. The Dutch
proband shows completely different
mutation bearing haplotypes, supporting this hypothesis.

25 The TD-2 proband was homozygous for all markers tested distal to
D9S127 but was heterozygous at D9S127 and DNA markers centromeric to it.
This suggested that the gene for TD was likely located to the genomic region
telomeric of D9S127 and encompassed by the markers demonstrating
homozygosity.

Mutation detection

Based on the defect in intracellular cholesterol transport in patients with TD, we reviewed the EST database for genes in this region which might be relevant to playing a role in this process. The *ABCI* transporter gene had previously been mapped to 9q31, but its precise physical location had not been determined (Luciani *et al.*, Genomics 21:150-159, 1994). The *ABCI* gene is a member of the ATP binding cassette transporters which represents a super family of highly conserved proteins involved in membrane transport of diverse substrates including amino acids, peptides, vitamins and steroid hormones (Luciani *et al.*, Genomics 21:150-159, 1994; Dean *et al.*, Curr. Opin. Gen. Dev. 5:779-785, 1995). Primers to the 3' UTR of this gene mapped to YACs spanning D9S306 (887-B2 and 930-D3) compatible with it being a strong candidate for TD. We initiated large scale genomic sequencing of BACs spanning approximately 800 kb around marker D9S306 (Research Genetics RPCI-11 BACs: 4I8, 31J20, 47O19, and 179G21, which are publically available from Research Genetics which is located at 2130 Memorial Parkway, Huntsville, Alabama 35801) BACs 4I8, 31J20, 47O19, and 179G21 are identical to previously described BACs 269, 274, 279 and 291, respectively (U.S.S.N. 09/526,193; U.S.S.N. 60/124,702; U.S.S.N. 60/138,048; U.S.S.N. 60/139,600; U.S.S.N. 60/151,977; Brooks-Wilson *et al.*, Nat. Genet. 22:336-345, 1999). The *ABCI* gene was revealed encompassing 49 exons and a minimum of 75 Kb of genomic sequence. In view of the potential function of a gene in this family as a cholesterol transporter, its expression in fibroblasts and localization to the minimal genomic segment underlying TD, we formally assessed ABC1 as a candidate.

Patient and control total fibroblast RNA was used in Northern blot analysis and RT-PCR and sequence analyses. RT-PCR and sequence analysis of TD-1 revealed a heterozygous T to C substitution in the TD-1 proband, which would result in a substitution of arginine for cysteine at a conserved

residue between mouse and man. This mutation, confirmed by sequencing exon 31 of the ABC1 gene, exhibited complete segregation with the phenotype on one side of this family. This substitution creates a *Hga*I site, allowing for RFLP analysis of amplified genomic DNA and confirmation of the mutation.

5 The point mutation in exon 31 was not seen on over 200 normal chromosomes from unaffected persons of Dutch decent, and 250 chromosomes of Western European decent, indicating it is unlikely to be a polymorphism. Northern blot analysis of fibroblast RNA from this patient, using a cDNA encompassing exons 2 to 50 of the gene, revealed a normal sized ~8 Kb transcript and a
10 truncated mutant transcript which was not visible in control RNA or in RNA from other patients with HDL deficiency. Additionally, Northern blot analysis using clones encompassing discrete regions of the cDNA revealed that the mutant transcript was detected with a cDNA compassing exons 2 to 50, 2 to 42, 2 to 23, much more faintly with a probe spanning exon 24 to 30, and not
15 seen with probes encompassing exons 31 to 43 or a probe spanning exons 31 to 50. This was repeated on multiple filters with control RNA, RNA from other patients with HDL deficiency and the other TD proband, and only in TD-1 was the truncated transcript observed. Sequence analysis of the coding region did not reveal an alteration in sequence that could account for this
20 finding. Furthermore, DNA analysis by Southern blot did not reveal any major rearrangements. Completion of exon sequencing in genomic DNA showed that this mutation was a G to C transversion at position (+1) of intron 24, affecting a splice donor site and causing aberrant splicing.

RT-PCR analysis of fibroblast RNA encoding the ABC1 gene from the
25 proband in TD-2 revealed a homozygous nucleotide change of A to G at nucleotide 1864 in exon 14, resulting in a substitution of arginine for glutamine at residue 597, occurring just proximal to the first predicted transmembrane domain of ABC1 at a residue conserved in mouse and as well as a *C. elegans* homolog. This mutation creates a second *Acc*I site within exon

14. Segregation analysis of the mutation in this family revealed complete concordance between the mutation and the low HDL phenotype as predicted. The proband in TD-2 is homozygous for this mutation, consistent with our expectation of a disease causing mutation in this consanguineous family.

5

Analysis of FHA families

Linkage analysis and refinement of the minimal genomic region containing the gene for FHA

Data from microsatellite typing of individual family members from the four pedigrees of French Canadian origin were analyzed. A maximum LOD score of 9.67 at a recombination fraction of 0.0 was detected at D9S277 on chromosome 9q31. Thereafter, 22 markers were typed in a region spanning 10 cM around this locus in these families. The frequency for these markers were estimated from a sample of unrelated and unaffected subjects of French ancestry.

15

TD and FHA have thus far been deemed distinct with separate clinical and biochemical characteristics. Even though the genes for these disorders mapped to the same region, it was uncertain whether FHA and TD were due to mutations in the same gene or, alternatively, due to mutations in genes in a similar region. Refinement of the region containing the gene for FHA was possible by examining haplotype sharing and identification of critical recombination events. Seven separate meiotic recombination events were seen in these families, clearly indicating that the minimal genomic region containing the potential disease gene was a region of approximately 4.4 cM genomic DNA spanned by marker D9S1690 and D9S1866. This region is consistent with the results of two point linkage analysis which revealed maximal LOD scores with markers D9S277 and D9S306 and essentially excluded the region centromeric to D9S1690 or telomeric to D9S1866. An 8th meiotic recombination event further refined the FHA region to distal to D9S277.

25

As described herein, the *ABCI* gene mapped within this interval. The overlapping genetic data strongly suggested that FHA may in fact be allelic to TD. Utilization of sets of genetic data from FHA and TD provided a telomeric boundary at D9S1866 (meiotic recombinant) and a centromeric marker at D9S127 based on the homozygosity data of TD-2. This refined the locus to approximately 1 mb between D9S127 and D9S1866. The *ABCI* gene mapped within this minimal region.

Mutation detection in FHA

Mutation assessment of the *ABCI* gene was undertaken in FHA-1. Using primers that spanned overlapping segments of the mRNA we performed RT-PCR analysis and subjected these fragments to mutational analysis. A deletion of three nucleotides is evident in the RT-PCR sequence of FHA-1 III.01, resulting in a loss of nucleotides 2151-2153 and deletion of a leucine (Δ L693) at amino acid position 693. This leucine is conserved in mouse and *C. elegans*. The alteration was detected in the RT-PCR products as well as in genomic sequence from exon 15 specific amplification. This mutation results in a loss of an *Eco*RI restriction site. Analysis of genomic DNA from the family indicated that the mutation segregated completely with the phenotype of HDL deficiency. The loss of the *Eco*RI site results in a larger fragment being remaining in persons heterozygous for this mutation. This mutation maps to the first putative transmembrane domain of ABC1 and was not seen in 130 chromosomes from persons of French Canadian descent nor seen in over 400 chromosomes from persons of other Western European ancestry.

A mutation has also been found in patient genomic DNA in pedigree FHA-3 from Quebec. The alteration, a 6 bp deletion of nucleotides 5752-5757 within exon 42, results in a deletion of amino acids 1893 (Glu) and 1894 (Asp). The deletion was detected as a double superimposed sequence starting from the point of the deletion, and was detected in sequence reads in both

directions. The deletion can be detected on 3% agarose or 10% polyacrylamide gels, and segregates with disease in FHA-3. It was not seen in 128 normal chromosomes of French-Canadian origin or in 434 other control chromosomes. Amino acids 1893 and 1894 are in a region of the ABC1 protein that is conserved between human, mouse, and *C. elegans*, implying that it is of functional importance.

An additional mutation has been found in patient genomic DNA in pedigree FHA-2 from Quebec. The alteration, a C to T transition at position 6504, converts an arginine at position 2144 to a STOP codon, causing truncation of the last 118 amino acids of the ABC1 protein. This alteration segregates with disease in family FHA-2.

Functional relationship between changes in ABC1 transcript levels and cholesterol efflux

Antisense approaches were undertaken to decrease the ABC1 transcript and assess the effect of alteration of the transcript on intracellular cholesterol transport. The use of antisense primers to the 5' end of ABC1 clearly resulted in a decrease to approximately 50% of normal RNA levels. This would be expected to mimic in part the loss of function due to mutations on one allele, similar to that seen in heterozygotes for TD and patients with FHA. Importantly, reduction in the mRNA for the ABC1 gene resulted in a significant reduction in cellular cholesterol efflux, further establishing the role of this protein in reverse cholesterol transport and providing evidence that the mutations detected are likely to constitute loss of function mutations. Furthermore, these data support the functional importance of the first 60 amino acids of the protein. Antisense oligonucleotide AN-6 is directed to the novel start codon 5' to the one indicated in AJ012376.1; this antisense oligonucleotide effectively suppresses efflux.

Polymorphisms in ABC1 5' regulatory region and 5' UTR

Several polymorphisms in the 5' regulatory region of human ABC1 (SEQ ID NO: 1) have been identified (Fig. 4). Because of their location, it is likely that ABC1 gene expression will differ among humans having different promoter polymorphisms, and these individuals may also respond differently to the same drug treatment. Thus, using these newly-identified polymorphisms, one can tailor drug treatment depending on which polymorphism(s) is/are present in a patient. The presence or absence of particular ABC1 polymorphisms may also be used in determining an individual's predisposition to developing CVD.

The methods of the invention may be performed using the following materials and methods.

Biochemical studies

Blood is withdrawn in EDTA-containing tubes for plasma lipid, lipoprotein cholesterol, ApoAI, and triglyceride analyses, as well as storage at -80°C. Leukocytes are isolated from the buffy coat for DNA extraction.

Lipoprotein measurement is performed on fresh plasma as described elsewhere (Rogler *et al.*, Arterioscler. Thromb. Vasc. Biol. 15:683-690, 1995). Lipids, cholesterol and triglyceride levels are determined in total plasma and plasma at density $d < 1.006$ g/mL (obtained after preparative ultracentrifugation) before and after precipitation with dextran manganese. Apolipoprotein measurement is performed by nephelometry for ApoB and ApoAI.

Genomic clone assembly and physical map construction of the 9q31 region

Using the Whitehead Institute/MIT Center for Genome Research map as a reference, the genetic markers of interest at 9q31 were identified within YAC contigs. Additional markers that mapped to the approximate 9q31 interval from public databases and the literature were then assayed against the YAC

clones by PCR and hybridization analysis. The order of markers was based on their presence or absence in the anchored YAC contigs and later in the BAC contig. Based on the haplotype analysis, the region between D9S277 and D9S306 was targeted for higher resolution physical mapping studies using
5 bacterial artificial chromosomes (BACs). BACs within the region of interest were isolated by hybridization of DNA marker probes and whole YACs to high-density filters containing clones from the RPCI-11 human BAC library.

Sequence retrieval and alignment

10 The human *ABC1* mRNA sequence was retrieved from GenBank using the Entrez nucleotide query (Baxevanis *et al.*, A Practical Guide to the Analysis of Genes and Proteins, eds. Baxevanis, A.D. & Ouellette, B.F.F. 98:120, 1998) as GenBank accession number AJ012376.1. The version of the protein sequence we used as wild-type (normal) was CAA10005.1.

15 We identified an additional 60 amino acids in-frame with the previously-believed start methionine. Bioinformatic analysis of the additional amino acids indicates the presence of a short stretch of basic amino acid residues, followed by a hydrophobic stretch, then several polar residues. This may represent a leader sequence, or another transmembrane or membrane-associated region of the *ABC1* protein. In order to differentiate among the
20 foregoing possibilities, antibodies directed to the region of amino acids 1-60 are raised against and used to determine the physical relationship of amino acids 1-60 in relation to the cell membrane. Other standard methods can also be employed, including, for example, expression of fusion proteins and cell
25 fractionation.

The mouse *ABC1* sequence used has accession number X75926. It is very likely that this mouse sequence is incomplete, as it lacks the additional 60 amino acids described herein for human *ABC1*.

Version 1.7 of ClustalW was used for multiple sequence alignments with BOXSHADE for graphical enhancement (http://www.isrec.isb-sib.ch:8080/software/BOX_form.html) with the default parameter. A *Caenorhabditis elegans* ABC1 orthologue was identified with BLAST (version 2.08) using CAA1005.1 (see above) as a query, with the default parameter except for doing an organism filter for *C. elegans*. The selected protein sequence has accession version number AAC69223.1 with a score of 375, and an E value of 103.

10 *Genomic DNA sequencing*

BAC DNA was extracted from bacterial cultures using NucleoBond Plasmid Maxi Kits (Clontech, Palo Alto, CA). For DNA sequencing, a sublibrary was first constructed from each of the BAC DNAs (Rowen *et al.*, Automated DNA Sequencing and Analysis, eds. Adams, M.D., Fields, C. & Venter, J.C., 1994). In brief, the BAC DNA was isolated and randomly sheared by nebulization. The sheared DNA was then size fractionated by agarose gel electrophoresis and fragments above 2 kb were collected, treated with Mung Bean nuclease followed by T4 DNA polymerase and klenow enzyme to ensure blunt-ends, and cloned into *Sma*I-cut M13mp19. Random clones were sequenced with an ABI373 or 377 sequencer and fluorescently labeled primers (Applied BioSystems, Foster City, CA). DNASTar software was used for gel trace analysis and contig assembly. All DNA sequences were examined against available public databases primarily using BLASTn with RepeatMasker (University of Washington). The sequence of each of the assembled contigs is shown in Figs. 1A-D.

Reverse transcription (RT)-PCR amplification and sequence analysis

Total RNA was isolated from the cultured fibroblasts of TD and FHA patients, and reverse transcribed with a CDS primer containing oligo d(T)18

using 250 units of SuperScript II reverse transcriptase (Life Technologies, Inc., Rockville, MD) as described (Zhang *et al.*, J. Biol. Chem. 27:1776-1783, 1996). cDNA was amplified with Taq DNA polymerase using primers derived from the published human *ABC1* cDNA sequence (Luciani *et al.*, Genomics 21:150-159, 1994). Six sets of primer pairs were designed to amplify each cDNA sample, generating six DNA fragments which are sequentially overlapped covering 135 to 7014 bp of the full-length human *ABC1* cDNA. The nucleotides are numbered according to the order of the published human cDNA sequence (AJ012376.1). Primer pairs (1): 135-158 (f) and 1183-1199 (r); (2): 1080-1107 (f) and 2247-2273 (r); (3): 2171-2197 (f) and 3376-3404 (r); (4): 3323-3353 (f) and 4587-4617 (r); (5) 4515-4539 (f) and 5782-5811 (r); (6): 5742-5769 (f) and 6985-7014 (r). RT-PCR products were purified by Qiagen spin columns. Sequencing was carried out in a Model 373A Automated DNA sequencer (Applied Biosystems) using Taq di-deoxy terminator cycle sequencing and Big Dye Kits according to the manufacturer's protocol.

Northern blot analysis

Northern transfer and hybridizations were performed essentially as described (Zhang *et al.*, J. Biol. Chem. 27:1776-1783, 1996). Briefly, 20 μ g of total fibroblast RNA samples were resolved by electrophoresis in a denaturing agarose (1.2%; w/v) gel in the presence of 7% formaldehyde, and transferred to nylon membranes. The filters were probed with 32 P-labeled human *ABC1* cDNA as indicated. Pre-hybridization and hybridizations were carried out in an ExpressHyb solution (ClonTech) at 68°C according to the manufacturer's protocol.

Cell culture

Skin fibroblast cultures are established from 3.0 mm punch biopsies of the forearm of FHD patients and healthy control subjects as described (Marcil *et al.*, Arterioscler. Thromb. Vasc. Biol. 19:159-169, 1999).

5

Cellular cholesterol labeling and loading

The protocol for cellular cholesterol efflux experiments has been described in detail elsewhere (Marcil *et al.*, Arterioscler. Thromb. Vasc. Biol. 19:159-169, 1999). The cells are ³H-cholesterol labeled during growth and free cholesterol loaded in growth arrest.

10

Cholesterol efflux studies

Efflux studies are carried out from 0 to 24 hours in the presence of purified ApoAI (10 µg protein/mL medium). Efflux is determined as a percent of free cholesterol in the medium after the cells were incubated for specified periods of time. All experiments are preferably performed in triplicate, in the presence of cells from one control subject and the cells from the study subjects to be examined.

15

Determination of genomic structure of the ABC1 gene

Most splice junction sequences were determined from genomic sequence generated from BAC clones spanning the ABC1 gene. More than 160 kb of genomic sequence were generated. Genomic sequences were aligned with cDNA sequences to identify intron/exon boundaries. In some cases, long distance PCR between adjacent exons was used to amplify intron/exon boundary sequences using amplification primers designed according to the cDNA sequence. The genomic sequence of human ABC1 is shown in Figs. 1A-D.

20

25

Analysis of ABC1 Heterozygotes

Identification of subjects

Subjects heterozygous for mutations in the ABC1 gene were individuals identified from the seven TD and FHA families previously described (Brooks-Wilson *et al.*, *supra*; Marcil *et al.*, *supra*). In addition, heterozygous individuals from three new Tangier disease families (TD3-5) and one new FHA kindred (FHA6) were included. The second mutation has not been identified in one of the TD kindreds (TD4); however, a marker immediately adjacent to ABC1 cosegregates with the low HDL phenotype. Individuals bearing the affected haplotype were considered heterozygotes. The presence or absence of mutations identified by genomic sequencing of probands from each family was subsequently confirmed by restriction fragment length polymorphism (RFLP) assays, to define heterozygous and unaffected individuals, respectively.

The control cohort consisted of unaffected members of the 11 families. These individuals share a genetic background with the heterozygotes, and environmental factors are expected to be similar amongst family members. Thus, many additional factors that influence HDL are controlled for, and the phenotypic differences between heterozygotes and unaffected individuals can be largely attributed to variation in ABC1 gene activity.

All subjects gave informed consent to their participation in this study, and the genetic analysis protocol was approved by the Ethics committees of the University of British Columbia, the Academic Medical Centre in Amsterdam and the Clinical Research Institute of Montreal (IRCM).

Lipid and cholesterol efflux measurements

Lipid levels in ABCA1 heterozygotes were measured as previously described (Brooks-Wilson *et al.*, *supra*; Marcil *et al.*, *supra*), at standardized lipid clinics in Vancouver, Montreal and Amsterdam. LDL was calculated by

the method of Friedewald *et al.* (Clin. Chem. 18:499-502, 1972), modified to account for lipid measurements in mmol/L.

Cellular cholesterol efflux from fibroblast cultures was measured as previously described (Brooks-Wilson *et al.*, *supra*; Marcil *et al.*, *supra*). Each experiment was performed in triplicate wells and averaged. Measurements are reported as the percentage efflux in each subject relative to an average of at least two healthy controls included within the same experiment. Individual experiments were repeated at least twice, and the average relative efflux over all experiments was used.

Statistics

In analysis of the heterozygotes, differences in mean baseline demographics and lipid levels between groups were compared by Student's t-test. Comparisons of frequency either between the male to female ratio or of distributions across various percentile ranges were made using the chi-square test. Analyses of potential interactions between affected status and either sex or BMI were performed using a general linear model. Statistical analysis was performed using Prism (version 3.00, Graphpad Software) or Systat (version 8.0, SPSS Inc.). All values are reported as mean \pm standard deviation.

Decreased HDL cholesterol and an increased risk for CAD in ABC1 heterozygotes

The analyzed cohort comprised 77 individuals from 11 families identified as heterozygous for mutations in the ABC1 gene. A comparison of mean lipid levels in heterozygotes with mean levels in all available unaffected family members (n=156) is presented in Fig. 6. Heterozygotes have an approximately 40-45% decrease in HDL and apoA-I and a mild (approximately 10%) decrease in apoA-II compared to unaffected family members. Mean triglycerides (TG) were increased by approximately 40% in heterozygotes

compared to unaffected family members, and were further increased in TD patients. Unlike TD patients, there is no significant decrease in either total cholesterol (TC) or LDL cholesterol in heterozygotes, and apoB levels were not different in heterozygotes from controls. Mean HDL levels in carriers of each of the mutations were similarly reduced by approximately 40-50% compared to unaffected family members (Fig. 9).

The heterozygote phenotype was further examined by calculating the percentage of individuals falling within a given range of age and sex specific percentiles (based on LRC criteria (Heiss *et al.*, *supra*; Heiss *et al.*, Circulation 61:302-315, 1980). Much variability in the heterozygote phenotype was evident. As illustrated in Fig. 5A, although a significantly higher percentage of heterozygotes had HDL cholesterol less than the 5th percentile for age and sex compared to unaffected controls (65% vs. 5%, $p < 0.0001$), 5% of the heterozygotes had HDL greater than the 20th percentile, with HDL ranging up to the 31st percentile for age and sex. Thus, in some individuals clearly the low HDL phenotype is less severe. A broad distribution of triglyceride (TG) levels was also evident (Fig. 5B). A significantly lower percentage of heterozygous individuals had TG below the 20th percentile for age and sex ($p = 0.03$), and a significantly larger percentage had TG >80th percentile ($p = 0.005$) compared to unaffected family members, but substantial overlap between the two distributions was seen.

Another important question is whether individuals heterozygous for ABC1 mutations are at an increased risk of developing coronary artery disease (CAD). In our large cohort, symptomatic vascular disease was over three times as frequent in the adult heterozygotes as in unaffected family members (Fig. 6). The forms of vascular disease were generally more severe in the heterozygotes than in their unaffected family members (Fig. 7). Heterozygotes had myocardial infarctions (five, one fatal) and severe vascular disease requiring multiple interventions, whereas in unaffected individuals, CAD was manifest

as angina in two cases and as a transient ischemic attack at the age of 80 in another. Furthermore, the mean age-of-onset was on average a decade younger in heterozygotes compared to unaffected controls (Fig. 6)

5 *Cholesterol efflux, HDL level, and CAD in ABC1 heterozygotes*

 We have previously shown that individuals heterozygous for ABC1 mutations have decreased cholesterol efflux. In the present study, the relationship between cholesterol efflux levels, HDL cholesterol levels, and CAD was further assessed. Relative cholesterol efflux in individuals heterozygous for an ABC1 mutation was plotted against the mean HDL cholesterol levels observed in the carriers of that mutation, expressed as a percentage of the unaffected members within that family (Fig. 8). Cholesterol efflux levels associated with each mutation strongly predict the corresponding HDL cholesterol levels in the families, accounting for 82% of the variation in HDL cholesterol ($r^2=0.82$, $p=0.005$). Furthermore, in one large family (FHA2), where efflux has been measured in three independent heterozygotes, an r^2 value of 0.81 was obtained when individual plasma HDL levels were plotted against individual efflux measurements. Using the regression equation of mean HDL levels in the heterozygotes on the efflux level of the heterozygous carrier ($p=0.02$), the relationship between expected changes in ABC1 efflux activity and HDL levels was estimated. Based on this analysis, we predict that each 8% change in efflux levels would be associated with a 0.1 mmol/L change in HDL cholesterol.

 Relative cholesterol efflux levels are also related to CAD within the family. Families with clearest evidence for premature CAD had individuals with the lowest cholesterol efflux (bold on Fig. 8 and Fig. 9). These data suggest that the level of residual ABC1 function is a critical determinant of both HDL cholesterol levels and susceptibility to CAD.

Comparison of mutation type and location to the severity of phenotype in individuals heterozygous for ABC1 mutations

We have previously noted that the phenotypic presentation of our FHA heterozygotes was more severe than that of our TD heterozygotes.

5 Furthermore, we initially noted more deletions and premature truncations of the protein in our FHA families than our TD families. Thus, as residual ABC1 activity is an important predictor of severity of the phenotype, the influence of the nature of the mutation on the phenotypic expression of mutations in the ABC1 gene was examined. Severe mutations which would be expected to
10 result in a non-functional allele were defined as deletions or mutations that caused premature truncation of the protein (frameshifts and nonsense mutations) or that disrupted natural splicing of the protein. Missense mutations, on the other hand, result in the change of only a single amino acid and may result in a protein product that still retains partial activity.

15 Lipid levels were compared in heterozygous carriers of severe and missense mutations. While there was a trend to decreased HDL levels in carriers of severe compared to missense mutations, this trend did not reach significance (Fig. 10). A range of HDL levels in individual missense and severe mutations were observed (Fig. 9). The M1091T missense mutation is
20 the most severe mutation in terms of effects on efflux and HDL levels, with a more severe phenotype than even early truncations of the protein (e.g. R909X).

The site of mutation (e.g. N-terminal or C-terminal) within the ABC1 protein did not influence the phenotype (Fig. 11). The presence of CAD is seen in carriers of mutations in several domains of the protein. Patients with
25 mutations on both alleles manifest with splenomegaly alone or in association with CAD (TD1). Thus the phenotype appears to be mutation specific, and most likely dependent on remaining ABC1 function of the wild-type allele and residual function of the mutant allele, similar to what has been shown for mutations in ABCR, a close homologue of ABC1 (van Driel *et al.*, Ophthalmic

Genet. 19:117-122, 1998).

Relationship between phenotype of mutations in the ABC1 gene and age

One factor influencing phenotypic expression that became apparent in the families was age. We first characterized the effect of age on the HDL levels of individuals in two previously reported families (Marcil *et al.*, *supra*) (Figs. 12A and 12B). In family FHA3, while heterozygous individuals in generations II and III all had HDL cholesterol levels less than the 5th percentile for age and sex, those in generation IV had a much more variable phenotype, with HDL cholesterol ranging up to the 20th percentile. In family FHA1, the same pattern was observed.

The distribution of individuals less than 30 years old across HDL percentile ranges was compared to the corresponding distribution of individuals 30-70 years old across HDL percentile ranges (Fig. 13). A significantly larger percentage of individuals 30-70 years old had HDL cholesterol less than the 5th percentile compared to the percentage of individuals less than 30 years old with HDL cholesterol less than the 5th percentile. Mean HDL decreases in heterozygotes greater than 30 years of age compared to those less than 30 years of age; in contrast, there is no significant change in unaffected controls (Fig. 14). Similar results are seen in males and females separately and in both pre- and post-menopausal ages in women (Figs. 15A and 15B). Triglyceride levels increase with age in both heterozygotes and unaffected family members.

Assessment of the influences of gender and BMI on the phenotypic expression of ABC1 mutations

Females are known to have elevated HDL and decreased triglyceride levels compared to males. Thus, the phenotype of ABC1 heterozygotes was analyzed to determine whether the phenotype was influenced by gender. HDL

cholesterol is significantly lower than unaffected controls in both heterozygous males and females (0.70 ± 0.24 versus 1.21 ± 0.29 , $p < 0.0001$; 0.76 ± 0.25 versus 1.41 ± 0.38 , $p < 0.0001$, respectively). This was reflected in decreased apoAI (0.92 ± 0.27 versus 1.36 ± 0.22 , $p < 0.0001$; 0.92 ± 0.36 versus 1.49 ± 0.28 , $p < 0.0001$ in males and females, respectively), and a trend towards a mild decrease in apoAII in both males and females compared to unaffected family members (0.35 ± 0.08 versus 0.40 ± 0.09 , $p = 0.08$; 0.35 ± 0.09 versus 0.39 ± 0.07 , $p = 0.06$, respectively). Triglycerides are higher in both male (2.07 ± 2.16 versus 1.30 ± 1.30 , $p = 0.02$) and female (1.34 ± 0.86 versus 1.09 ± 0.63 , $p = 0.08$) heterozygotes compared to unaffected family members. The difference in HDL between males and females was reduced in heterozygotes compared to controls ($p = 0.11$), while the difference in triglycerides was increased compared to controls ($p = 0.13$).

Another factor known to influence HDL and triglyceride levels is BMI. The entire cohort was divided into tertiles of BMI, and the mean HDL and triglyceride levels of heterozygotes and unaffected individuals by BMI tertile are shown in Figs. 16A and 16B. BMI had a significant effect on both HDL and triglycerides in both heterozygotes and controls ($p < 0.0001$). The effect of BMI on HDL-C and triglyceride levels was more severe in heterozygotes for ABC1 than in controls, being evident at lower BMIs (mid-tertile) in heterozygotes. A raised BMI was more obviously associated with changes in HDL and triglyceride levels in heterozygotes compared to controls. However, neither effect reached statistical significance. HDL was reduced in heterozygotes compared to controls in all BMI tertiles ($p < 0.0001$ in each tertile). While triglyceride levels were increased in all BMI tertiles in heterozygotes compared to unaffected family members, this difference was only significant in the middle BMI tertile ($p = 0.009$).

Analysis of ABC1 SNPs from REGRESS Study

Identification of SNPs

SNPs in the ABC1 gene were identified during the complete genomic sequencing of 14 unrelated probands with low HDL-C (Brooks-Wilson *et al.*,
5 *supra* 1999; Marcil *et al.*, *supra* 1999). Variants that were identified within the low HDL families that did not co-segregate with the low HDL phenotype or that were observed in unaffected individuals were assumed to be SNPs. Based on the sequencing of BAC clones spanning the entire ABC1 region (described above), sites identified as heterozygous or different from that found
10 in sequenced individuals were also identified as polymorphisms. Sequence data was available from at least one control individual at all variant coding sites. The SNPs are numbered from the nucleotide described as position 1 (Pullinger *et al.*, Biochemical and Biophysical Research Communications 271:451-455, 2000), naming the first exon number 1. As a standardized
15 nomenclature for all variants, the "wild-type" allele (more frequent in the REGRESS population) is designated A, while the variant (less frequent) allele is designated B.

Subjects

20 To assess the effects of these SNPs on lipid levels and CAD, we studied a cohort of 804 men with proven coronary artery disease who participated in the Regression Growth Evaluation Statin Study (REGRESS), which has previously been described in detail (Jukema *et al.*, Circulation 91:2528-2540, 1995). Briefly, study participants were required to have at least one coronary
25 artery with a stenosis of more than 50% as assessed by coronary angiography, a plasma total cholesterol concentration of 4 to 8 mmol/L (155 to 310 mg/dL), and a plasma triglyceride concentration below 4 mmol/L (350 mg/dL). Phenotypic effects of the cSNPs were examined in relationship to baseline lipid parameters.

Patients were randomly assigned to treatment with pravastatin (Pravachol, Bristol-Myers Squibb, Princeton, N.J.) or placebo for a period of two years. Computer-assisted quantitative coronary angiography was carried out at the start and at the end of the study as previously described (Jukema *et al.*, *supra* (1995)). The baseline values and changes in the average mean segment diameter (MSD), which is a measurement of the average unobstructed diameter along the vessel, and in the minimal obstructive diameter (MOD), which is a measurement of the smallest unobstructed segment, were used as the primary measures of CAD. The MSD reflects diffuse changes of atherosclerosis, and the MOD reflects focal atherosclerotic changes. Larger MSD and MOD measurements reflect less occlusion of the vessel, and a decrease in these parameters reflects progression of coronary atherosclerosis. In addition, the prevalence of coronary events; defined as death, myocardial infarction, unscheduled coronary angioplasty or bypass surgery (PTCA, CABG), or stroke/transient ischemic attack; was examined.

Blood was collected from each patient at baseline, and DNA was extracted according to standard procedures. Several subsequent genetic studies have been performed on this cohort (Reymer *et al.*, *Nature Genetics* 10:28-34, 1995; Jukema *et al.*, *Circulation* 94:1913-1918, 1996; Kluijtmans *et al.*, *Circulation* 96:2573-2577, 1997; Kastelein *et al.*, *Clinical Genetics* 53:27-33, 1998; Kuivenhoven *et al.*, *New England Journal of Medicine* 338:86-93, 1998). The REGRESS and its DNA substudies were approved by all seven institutional review boards of the participating centers and by their medical ethics committees.

Additional Dutch subjects with low HDL and premature coronary artery disease were obtained from previously described populations (Kuivenhoven *et al.*, *Arteriosclerosis, Thrombosis and Vascular Biology* 17:560-568, 1997; Verhoff *et al.*, *Atherosclerosis* 141:161-166 1998; Franco *et al.*, *British Journal of Hematology* 102:1172-1175, 1998; Wittekoek *et al.*,

Artherosclerosis 146:271-279, 1999; Franko *et al.*, British Journal of Hematology 104:50-54, 1999). Dutch control subjects were taken from a large population based study designed to assess the effects of various risk factors on CAD (Seidell *et al.*, International Journals of Obesity 19:924-927 1995; Kuivenhoven *et al.* Arteriosclerosis, Thrombosis and Vascular Biology 17:595-599, 1997). French Canadian subjects were a random sample of individuals. The South African Black and Cantonese cohorts have previously been described (Ehrenborg *et al.*, Arteriosclerosis, Thrombosis and Vascular Biology 17:2672-2678, 1997). All subjects gave informed consent.

cSNP screening

For each variant, a restriction enzyme whose cleavage pattern was altered by the variant was identified for development of an RFLP assay. If no suitable enzyme was found, a mismatch strategy was employed, whereby a single nucleotide mismatch was incorporated into the PCR primer, creating a restriction site in combination with either the wild-type or variant allele. The specific conditions of all assays are described in Fig. 17. All PCR reactions were carried out in 50 μ L volumes, in the presence of 1x PCR buffer and 1.5 μ M MgCl₂ (Life Technologies). Thermocycling parameters for all assays were as follows: 95°C for 3 min; 35 cycles of denaturation at 95°C for 10 seconds, annealing for 30 seconds at the temperature specified in Fig. 17, and elongation for 30 seconds at 72°C; and a final elongation at 72°C for 10 min. All digestions (15-20 μ L PCR product) were carried out in manufacturer's buffer (New England Biolabs) for 2 hours at the temperature specified by the manufacturer. As an example, the digest results for the R219K are shown in Fig. 18. A 177 base pair fragment with the A allele is not cut by *Eco*NI, whereas the B allele is digested to produce fragments of 107 and 70 base pairs. Heterozygous individuals thus display all three bands (177, 107, and 70 base pairs).

Genotyping with the TaqMan(r) assay

To facilitate the mass screening of some variants, TaqMan based polymerase chain reaction (PCR) assays (Holland *et al.*, Proc.Natl.Acad.Sci. 88 (16):7276-7280, 1991; Lee *et al.*, Nucleic Acids Research 21 (16):3761-3766, 1993) were developed for the detection of polymorphisms in the ABC1 gene. In this one-tube assay, two fluorogenic hybridization probes (one for each allele) are labeled with different fluorescent reporter dyes (FAM or TET) at their 5' terminus and a common quencher dye (TAMRA) at their 3' terminus. These probes are cleaved by the 5' nuclease activity of Taq enzyme during PCR amplification. This cleavage separates the reporter from the quencher dye and generates an increase in reporter fluorescence. By using two different reporter dyes, cleavage of allele-specific probes can be detected in a single PCR. The difference in the measured fluorescence intensity between the two TaqMan probes allows for accurate allele calling.

PCR amplifications with flanking sets of primers (300 nM) in the presence of two TaqMan probes (25 nM each) and 4.5 mM MgCl₂ were performed using the following thermocycling protocol: initial denaturation at 96°C for 10 min, followed by 39 cycles of 96°C for 30 sec, 63°C for 1 min and 72°C for 15 sec, followed by a final extension at 72°C for 10 min. Each plate included controls (no DNA template) as well as standards of each known genotype. Fluorescence quantification and genotype determination were performed on a Perkin Elmer LS50B or ABI Prism 7700 Sequence Detector. The fluorescence from each reaction was normalized to the signal from the no-template controls.

Cellular cholesterol efflux studies

Cellular cholesterol efflux from fibroblast cultures was measured as described above in the "Analysis of ABC1 Heterozygotes" section.

Statistics

Within the REGRESS population, the baseline characteristics of the patients in the three genotypes (AA, AB, BB) was compared using one way analysis of variance and the chi-square test, where appropriate. In cases where the BB genotype was rare, the AA group was compared to the combined group AB+BB. The cumulative coronary event incidence in these genotypic groups was compared using the logrank test. The relation between age and HDL level was investigated using a linear regression model, and the difference between genotypes with respect to the slopes of this regression line was tested using covariance analysis. In addition to this regression analysis, the R219K genotypes were compared among age-defined subgroups. Randomization to placebo and pravastatin was assessed by chi square analysis and was equivalent in all genotypic groups for all variants except the R1587K variant. For this variant, a lower proportion of carriers was randomized to pravastatin treatment. In addition, change in MOD, MSD, and prevalence of coronary events (the three variables measured during the trial and thus following randomization) were analyzed for the placebo and pravastatin subgroups separately. Similar genotypic effects for each of the variants were observed in the treatment subgroups (i.e. the pravastatin and placebo control groups).

All lipid levels are reported in mmol/L. All values are reported as mean \pm standard deviation.

Association of R219K polymorphism with reduced triglyceride levels and a decreased risk of CAD

The common R219K polymorphism results in the substitution of a lysine for an arginine at amino acid 219 of the ABC1 protein. The allele frequency of the variant, or "B", allele was 0.25, and its carrier frequency was 46.3%, as shown in Fig. 19.

The relationship between this polymorphism and CAD was examined. The B allele of the R219K polymorphism was associated with decreased baseline CAD. Both the MSD and the MOD, were significantly increased in an allele-dose dependent fashion from AA to AB to BB (Fig. 20).

5 The angiographic data was paralleled by differences in clinical coronary events rates. A smaller percentage of individuals homozygous for the rarer B allele (BB) had had a myocardial infarction (MI) prior to the initiation of the trial. Carriers of the B allele exhibited a strong trend towards an increased prevalence of no events over the course of the study (Fig. 21, $p=0.07$).

10 The association of the R219K polymorphism with reduced CAD was further supported by the reduced frequency of this allele in the REGRESS cohort which was selected for CAD. In fact, the genotype frequencies observed for this variant are not consistent with Hardy-Weinberg equilibrium ($p=0.004$). There are fewer BB individuals and more AB individuals than
15 would be expected (424 AA, 330 AB, and 36 BB individuals were observed compared to the expected 439 AA, 300 AB, and 51 BB individuals). As the REGRESS cohort was selected for men with CAD, the lack of Hardy-Weinberg equilibrium suggests that there was a preferential selection against BB individuals, consistent with the reduced CAD observed in this
20 group.

There were no obvious differences in mean HDL-C levels between the genotypes in the groups as a whole (Fig. 22); however, triglycerides were significantly lower in the carriers of the B allele. This suggests that ABC1 function may also directly influence plasma triglyceride levels, and that this
25 variant may be associated with a gain of ABC1 function. These findings are also consistent with the decreased CAD observed in carriers, suggesting that ABC1 modulation of triglyceride levels may be another mechanism whereby ABC1 activity influences risk of CAD.

To further explore the apparent lack of effect of this variant on HDL-C, the relationship between R219K genotype and HDL at various ages was examined. In younger individuals, the carriers of the B allele had increased HDL-C compared to non-carriers (Fig. 23). Furthermore, while HDL-C increased with age in the AA individuals, heterozygous carriers showed a much milder increase, and HDL cholesterol decreased with age in homozygous carriers (Fig. 24). In the AA individuals, HDL cholesterol is positively correlated with age ($p < 0.001$). In contrast, this relation was not apparent in individuals heterozygous for this variant, and HDL cholesterol was negatively correlated with age in the BB homozygotes, although neither the correlation for AB nor the correlation for BB individuals was statistically different from zero (Fig. 25A). The age-related increase in HDL-C in AA individuals is not maintained in carriers of the B allele (p value comparing slopes=0.04). Thus, the decreased CAD in carriers of the R219K may also be related to the fact that for the majority of their lifetime, carriers have had increased HDL-C compared to non-carriers.

The changes in HDL-C with age in the various R219K genotypes are mirrored by similar trends in the changes in cholesterol efflux with age (Fig. 25B). We have genotyped this variant in all individuals in whom we have measured efflux and who do not possess an ABC1 mutation. In AA individuals ($n=30$), cholesterol efflux increases with age, whereas in AB and BB individuals ($n=24$), efflux decreases with age (p -value comparing slopes=0.15). Thus, the differential age-related changes in HDL seen in the different R219K genotypes are consistent with similar functional changes in ABC1 activity.

From Fig. 23 it can be seen that triglyceride levels generally decrease with age, a finding seen in all R219K genotypes. The percent decrease in triglyceride levels was nearly half in carriers (9.3%) compared to non-carriers (17.3%, $p=0.07$). Differences between the genotypes are also observed in the

MSD and MOD. In the non-carriers, MSD and MOD measurements decrease significantly with age, reflecting increased atherosclerosis in the older individuals (Figs. 23 and 26). In contrast, in carriers of the R219K variant, these measurements do not significantly change with age. Thus, vascular disease progresses much more slowly with age in carriers of the R219K variant compared to non-carriers.

Populations of Asian and African origins have been shown to have increased HDL-C, decreased triglyceride levels, and decreased risk of CAD compared to Caucasian populations (Tyroler *et al.*, Circulation 62 (Suppl. IV):IV-99-IV-107, 1980; Tao *et al.*, International Journal of Epidemiology 21 (5):893-903, 1992; Brown *et al.*, Arteriosclerosis and Thrombosis 13:1139-1158, 1993; Adedeji, Tropical and Geographical Medicine 46 (1):23-26, 1994; Simon *et al.*, American Journal of Public Health 85 (12):1698-1702, 1995; Morrison *et al.*, Metabolism 47 (5):514-521, 1998), a finding paralleling the phenotypic effects of this variant. Thus, as SNP frequencies can often differ within different ethnic groups, the frequency of this variant within these two population groups was examined (Fig. 27). This variant is seen much more commonly in individuals of either Cantonese or South African Black descent, in which it is the predominant allele. This suggests that the increased frequency of this variant may in part account for the increased HDL, decreased triglyceride levels, and decreased CAD observed in these populations compared to Caucasian populations.

Effect of other cSNPs on plasma lipid levels and risk of CAD

No significant differences in lipid levels or CAD compared to respective non-carriers have been observed for carriers of the T774P (n=4), K776N (n=3) or E1172D variants (n=34). Carriers of the V825I (n=103 AB, 4 BB) had no obvious differences in lipid levels or baseline MSD or MOD. Carriers of the V825I variant did, however, have a significantly increased

number of events during the trial (44% versus 33%, $p=0.001$).

No carriers of the S1731C variant were detected in the REGRESS population, but this variant was found in one of our FHA families (FHA2). In individuals heterozygous for ABC1 mutations, this variant was associated with significantly decreased HDL-C (0.16 ± 0.04 , $n=2$ versus 0.64 ± 0.14 , $n=10$; $p=0.0009$ in carriers versus non-carriers). In unaffected family members, however, while carriers of the S1731C had lower HDL-C compared to non-carriers (1.03 ± 0.22 versus 1.09 ± 0.23), this was not statistically significant. The control individual in whom this variant was also seen (Fig. 19) had low plasma HDL-C (0.72 mmol/L).

Similar to carriers of the R219K, carriers of the V771M variant ($n=37$), had no difference in HDL-C compared to non-carriers; however, a marginally significant interaction between age and genotype on HDL-C levels was noted ($p=0.05$). All but 2 carriers of the V771M variant are also carriers of the R219K variant. The interaction between age and genotype on HDL-C remains nearly significant when adjusted for R219K genotype ($p=0.11$), thus this variant may have an age effect independent of that which can be attributed to the R219K. A trend to less CAD (increased MOD) was observed in carriers of this variant compared to non-carriers (1.89 ± 0.38 versus 1.76 ± 0.35 , $p=0.13$).

For the I883M cSNP, homozygous BB individuals ($n=14$) have increased progression in MOD (mean change of 0.53 ± 0.79 versus 0.11 ± 0.25 , $p<0.001$). BB individuals had an events rate double that of the AA individuals (21.4% versus 10.6%) although this was not statistically significant ($p=0.19$). No difference was observed in mean lipid levels between the I883M genotypes. Furthermore, there were significantly more BB individuals than expected under Hardy-Weinberg equilibrium (14 BB, 86 AB, and 320 AA individuals observed compared to the expected 8 BB, 98 AB, and 314 AA individuals). As this cohort was selected for individuals with CAD, this might suggest a preferential inclusion of those with the BB genotype. The

association of this variant with CAD is further supported by the significantly increased frequency of this variant in the premature CAD population (odds ratio for CAD in carriers of this variant= 0.43, 95% confidence interval 0.22-0.85, $p=0.01$) (Fig. 19). These findings contrast with those of a very recent report which suggests that the homozygous carriers of this cSNP have increased HDL-C (Wang *et al.*, Arteriosclerosis, Thrombosis and Vascular Biology 20:1983-1989, 2000).

Carriers of the V399A (AB, $n=9$) had a trend to higher HDL-C (1.03 ± 0.28 versus 0.92 ± 0.23 , $p=0.15$) compared to individuals who were AA at this site ($n=540$). No events were observed in the AB group (compared to 14% in AA's, $p=NS$), and carriers had half the prevalence of a family history of CAD (22.2% versus 49.4%, $p=0.18$). Furthermore, consistent with this data, the carriers had a trend to increased baseline MOD (1.92 ± 0.32 versus 1.73 ± 0.35 , $p=0.13$) and to less progression in MSD (-0.05 ± 0.10 versus 0.08 ± 0.19 , $p=0.16$) during the trial. However, as the number of carriers of small, firm conclusions regarding the relationship of this variant to increased HDL-C and decreased CAD cannot be drawn.

Carriers of the R1587K variant (AB, BB) have decreased HDL-C compared to non-carriers in an allele-dose dependent trend (0.86 ± 0.16 , 0.91 ± 0.23 , and 0.94 ± 0.23 for BB, AB, and AA, respectively, $p=0.03$). No significant interaction with age was noted ($p=0.32$). Furthermore, on multiple regression including age, BMI, smoking, and triglyceride levels as covariates, the R1587K genotype is a significant predictor of HDL-C ($p=0.027$). However, no significant differences in CAD or events during the trial were evident in carriers compared to non-carriers.

Summary of Association Studies of ABC1 Gene Variants and HDL Levels or Cardiovascular Disease

The following polymorphisms have been examined for their effect on cholesterol regulation and the predisposition for the development of cardiovascular disease. The polymorphisms are numbered from the nucleotide described as position 1 (Pullinger *et al.*, *supra*), naming the first exon number 1.

Substitution of A for G at nucleotide 1051 (R219K). Carriers of this variant have reduced triglyceride levels, increased HDL cholesterol levels (particularly in younger individuals), and reduced CAD.

Substitution of C for T at nucleotide 1591 (V399A). This variant was associated with a trend towards increased HDL cholesterol in carriers.

Substitution of A for G at nucleotide 2706 (V771M). Carriers of this variant have been shown to have decreased CAD.

Substitution of C for A at nucleotide 2715 (T774P). This variant was seen less often in individuals with low HDL cholesterol levels or CAD than in controls.

Substitution of C for G at nucleotide 2723 (K776N). This variant has been found at a lower frequency (0.54% versus 1.89%) in a coronary artery disease population versus a control population of similar Dutch background.

Substitution of C for G at nucleotide 3911 (E1172D). This variant is seen at lower frequencies in individuals with low HDL and in some populations with premature coronary artery disease.

Substitution of A for G at nucleotide 5155 (R1587K). This variant is associated with decreased HDL cholesterol levels in carriers.

Substitution of G for C at nucleotide 5587 (S1731C). Two FHA individuals who have this variant on the other allele have much lower HDL cholesterol (0.155 ± 0.025) than the FHA individuals in the family who do not have this variant on the other allele (0.64 ± 0.14 , $p=0.0009$). This variant has

also been found in one general population French Canadian control with HDL at the 8th percentile (0.92) and one French Canadian individual from a population selected for low HDL cholesterol levels and coronary disease (0.72).

5 *Substitution of G for A at nucleotide 2723 (I883M).* This variant has been seen at a much higher frequency in individuals of Dutch ancestry with premature coronary artery disease. Furthermore, homozygous carriers of this variant have significantly increased CAD progression compared to non-carriers.

10 *Substitution of A for G at nucleotide 2868 (V825I).* Carriers of this variant had significantly more CAD events than individuals who do not have this variant.

Substitution of C for G at nucleotide -191. Homozygous carriers of this variant have a three-fold increase in the frequency of coronary events (33.3% versus 11.2%, $p=0.003$) and a nearly double frequency of a positive family history of CAD (73.3% versus 47.7%, $p=0.01$).

15 *Substitution of G for C at nucleotide -17.* Carriers of this variant have significantly decreased coronary events (12.3% versus 18.2%, $p=0.04$) and a significantly decreased incidence of myocardial infarction (heart attack, 43.6% versus 52.8%, $p=0.02$).

20 *Substitution of T for C at nucleotide 69.* Carriers of this variant have increased CAD progression compared to non-carriers.

Substitution of G for C at nucleotide 127. Carriers of this variant have a trend towards decreased progression of CAD compared to non-carriers.

25 *Insertion of CCCT at nucleotide -1163 in intron 1.* Carriers of this variant have a trend to lower HDL cholesterol levels.

Substitution of G for A at nucleotide -1095 in intron 1. Homozygous carriers of this variant have a trend towards decreased HDL cholesterol and increased triglyceride levels compared to non-carriers.

Substitution of A for G at nucleotide -1027 in intron 1. Carriers of this variant are also carriers of the G(-720)A. Thus the effects attributed to that variant may also be attributed to carriers of this variant.

Substitution of A for G at nucleotide -720 in intron 1. Homozygous carriers of this variant had a trend towards an increased frequency of a positive family history of myocardial infarction.

Substitution of C for A at nucleotide -461 in intron 1. Carriers of this variant are also carriers of the A(-362)G. Thus the effects attributed to that variant may also be attributed to carriers of this variant.

Substitution of G for A at nucleotide -362 in intron 1. Carriers of this variant have decreased triglyceride levels compared to non-carriers.

Insertion of G at nucleotide 319. Carriers of this variant have increased CAD compared to non-carriers.

Substitution of G for C at nucleotide 378. Carriers of this variant are also carriers of the InsG319. Thus the effects attributed to that variant may also be attributed to carriers of this variant.

Functional Role of LXRE Binding Sites in ABC1 Genomic Sequence

The functional role of three of the LXRE consensus binding sites identified in the ABC1 genomic sequence of SEQ ID NO: 1 was confirmed using standard gel shift assay experiments. Briefly, the sequences of the LXRE consensus binding sites located at -4389 and -1641 of the promoter region, +4 of exon 1, and -7670 and -7188 of 3' intron 1 (Figure 3) were tested in gel shift assays using the cyp7 LXRE described by Lehmann *et al.* as a positive control (Lehmann *et al.*, J. Biol. Chem. 272:3137-3140, 1997).

In the first gel shift assay, binding of the labeled cyp7 LXRE probe was competed by a 400-fold excess of cold cyp7 probe, -4389 probe, -1641 probe, +4 probe, or -7670 probe. The signal disappeared completely in all cases.

For the next assay, the -4389, -1641, +4, -7670 and -7188 probes were labeled and binding to LXR-RXR complex was assayed. A signal similar to that of the positive control was observed for each of ABC1 LXRE probes, although the signal was slightly more intense for the +4 probe.

5 A competition assay was also performed using lesser quantities of each cold probe, i.e. 5-fold, 25-fold, and 50-fold more cold probe than labeled cyp7 probe. There was a dose dependant decrease in the signal for each of the probes. This decrease was more significant for the +4 and -7670 probes. Moreover, the signal was not modified by competition with a cold Dr2 like
10 probe, suggesting that the competition effect is indeed specific.

Thus, each of the tested potential LXRE binding sites seem to bind an *in vitro* LXR-RXR heterodimer. The LXRE binding site at +4 in exon 1 appears to have the highest affinity, closely followed by the LXRE binding site at -7670 in 3' intron 1.

15

Agonists and Antagonists

Useful therapeutic compounds include those which modulate the expression, activity, or stability of ABC1. To isolate such compounds, ABC1 expression, biological activity, or regulated catabolism is measured following
20 the addition of candidate compounds to a culture medium of ABC1-expressing cells. Alternatively, the candidate compounds may be directly administered to animals (for example mice, pigs, or chickens) and used to screen for their effects on ABC1 expression.

In addition its role in the regulation of cholesterol, ABC1 also
25 participates in other biological processes for which the development of ABC1 modulators would be useful. In one example, ABC1 transports interleukin-1 β (IL-1 β) across the cell membrane and out of cells. IL-1 β is a precursor of the inflammatory response and, as such, inhibitors or antagonists of ABC1 expression or biological activity may be useful in the treatment of any

inflammatory disorders, including but not limited to rheumatoid arthritis, systemic lupus erythematosus (SLE), hypo- or hyper- thyroidism, inflammatory bowel disease, and diabetes mellitus. In another example, ABC1 expressed in macrophages has been shown to be engaged in the engulfment and clearance of dead cells. The ability of macrophages to ingest these apoptotic bodies is impaired after antibody-mediated blockade of ABC1. Accordingly, compounds that modulate ABC1 expression, stability, or biological activity would be useful for the treatment of these disorders.

ABC1 expression is measured, for example, by standard Northern blot analysis using an *ABC1* nucleic acid sequence (or fragment thereof) as a hybridization probe, or by Western blot using an anti-ABC1 antibody and standard techniques. The level of ABC1 expression in the presence of the candidate molecule is compared to the level measured for the same cells, in the same culture medium, or in a parallel set of test animals, but in the absence of the candidate molecule. ABC1 activity can also be measured using the cholesterol efflux assay.

Transcriptional Regulation of ABC1 Expression

ABC1 mRNA is increased approximately 8-fold upon cholesterol loading. This increase is likely controlled at the transcriptional level. Using the genomic sequence described herein, one can identify transcription factors that bind to the 5' regulatory sequence by performing, for example, gel shift assays, DNase protection assays, or *in vitro* or *in vivo* reporter gene-based assays. The identified transcription factors are themselves drug targets. In the case of ABC1, drug compounds that act through modulation of transcription of ABC1 could be used for HDL modulation, triglyceride modulation, atherosclerosis prevention, and the treatment of cardiovascular disease. For example, using a compound to inhibit a transcription factor that represses ABC1 would be expected to result in up-regulation of ABC1 and, therefore,

up-regulation of HDL cholesterol levels and down-regulation of triglyceride levels. In another example, a compound that increases transcription factor expression or activity would also increase ABC1 expression, increase HDL levels, and decrease triglyceride levels.

5 Transcription factors known to regulate other genes in the regulation of apolipoprotein genes or other cholesterol- or lipid-regulating genes are of particular relevance. Such factors include, but are not limited to, the steroid response element binding proteins (SREBP-1 and SREBP-2), and the PPAR (peroxisomal proliferation-activated receptor), RXR, and LXR transcription
10 factors. Several consensus sites for certain elements are present in the sequenced region 5' to the ABC1 gene (Fig.3) and thus are likely to modulate ABC1 expression. For example, LXRs may alter transcription of ABC1 by mechanisms including heterodimerization with retinoid X receptors (RXRs) and then binding to specific response elements (LXREs). Examples of such
15 LXRs include LXR α and LXR β . Compounds that modulate LXR-mediated transcriptional activation are likely to modulate ABC1 gene expression and thus are useful for modulating HDL cholesterol levels and triglyceride levels. Janowski *et al.* (Proc. Natl. Acad. Sci. USA 96:266-271, 1999) described the role of naturally occurring oxysterols in LXR-dependent transactivation
20 through the promoter for cholesterol 7 α -hydroxylase (Cyp7 α), which is the rate limiting enzyme in bile acid synthesis. Janowski further demonstrated that oxysterols bind directly to LXRs. The position specific mono-oxidation of the sterol side chain is required for LXR high affinity binding and activation. Enhanced binding could be achieved by use of 24-oxo ligands. Oxygens at
25 more than one carbon on the side chain of cholesterol diminished LXR binding and activation as compared to monooxygenated analogs. LXR ligands were found to require a single stereoselective oxygen on the sterol side chain that functioned as a hydrogen acceptor. Introduction of dimethylamide exhibited the greatest binding and activation compared to an ester or carbonyl group.

Additional transcription factors which may also have an effect in modulating ABC1 gene expression and thereby HDL levels, triglyceride levels, atherosclerosis, and CAD risk include REV-ERB α , SREBP-1 & 2, ADD-1, EBP α , CREB binding protein, P300, HNF 4, RAR, and ROR α .. Exemplary binding sites are depicted in Fig. 3. Additional binding sites for these factors can be found, for example, through examination of the sequence in SEQ ID NO: 1.

RXR heterodimerizes with many nuclear receptors, including LXR, and aids in transactivating the target gene. Thus, compounds that modulate RXR-mediated transcriptional activity will also modulate ABC1 expression. Numerous RXR-modulating compounds (rexinoid compounds) are known in the art, including, for example, hetero ethylene derivatives; tricyclic retinoids; trienoic retinoids; benzocycloalkenyl-alka:di- or trienoic acid derivatives; bicyclic-aromatic compounds and their derivatives; bicycylmethyl-aryl acid derivatives; phenyl-methyl heterocyclic compounds; tetrahydro-naphthyl compounds; arylthio-tetrahydro-naphthalene derivatives and heterocyclic analogues; 2,4-pentadienoic acid derivatives; tetralin-based compounds; nonatetraenoic acid derivatives; SR11237; dexamethasone; hydroxy, epoxy, and carboxy derivatives of methoprene; bicyclic benzyl, pyridinyl, thiophene, furanyl, and pyrrole derivatives; benzofuran-acrylic acid derivatives; aryl-substituted and aryl and (3-oxo-1-propenyl)-substituted benzopyran, benzothiopyran, 1,2-dihydroquinoline, and 5,6-dihydronaphthalene derivatives; vitamin D3 (1,25-dihydroxyvitamin D3) and analogs; 24-hydroxylase inhibitor; mono-or polyenic carboxylic acid derivatives; tetrahydroquinolin-2-one-6 or 7-yl and related derivatives; tetrahydronaphthalene; oxyiminoalkanoic acid derivatives; LG 100268; and LGD 1069. Additional compounds include BRL 49653; troglitazone; pioglitazone; ciglitazone; WAY-120; englitazone; AD 5075; and darglitazone.

PPARs may alter transcription of ABC1 by mechanisms including heterodimerization with retinoid X receptors (RXRs) and then binding to specific proliferator response elements (PPREs). Examples of such PPARs include PPAR α , β , γ and δ . These distinct PPARs have been shown to have transcriptional regulatory effects on different genes. PPAR α is expressed mainly in liver, whereas PPAR γ is expressed in predominantly in adipocytes. Both PPAR α and PPAR γ are found in coronary and carotid artery atherosclerotic plaques and in endothelial cells, smooth muscle cells, monocytes and monocyte-derived macrophages. Activation of PPAR α results in altered lipoprotein metabolism through PPAR α 's effect on genes such as lipoprotein lipase (LPL), apolipoprotein CIII (apo CIII) and apolipoprotein AI (apo AI) and AII (apo AII). PPAR α activation results in overexpression of LPL and apoA-I and apoA-II, but inhibits the expression of apo CIII. PPAR α activation also inhibits inflammation, stimulates lipid oxidation and increases the hepatic uptake and esterification of free fatty acids (FFA's). PPAR α and PPAR γ activation may inhibit nitric oxide (NO) synthase in macrophages and prevent interleukin-1 (IL-1) induced expression of IL-6 and cyclo-oxygenase-2 (COX-2) and thrombin induced endothelin-1 expression secondary to negative transcriptional regulation of NF-KB and activation of protein-1 signaling pathway. It has also been shown that PPAR α induces apoptosis in monocyte-derived macrophages through the inhibition of NF-KB activity.

Activation of PPAR α can be achieved by compounds such as fibrates, β -estradiol, arachidonic acid derivatives, WY-14,643 and LTB₄ or 8(s)HETE. PPAR γ activation can be achieved through compounds such as thiozolidinedione antidiabetic drugs, 9-HODE and 13-HODE. Additional compounds such as nicotinic acid or HMG CoA reductase inhibitors may also alter the activity of PPARs.

ABC transporters have been shown to increase the uptake of long chain fatty acids from the cytosol to peroxisomes and, moreover, to play a role in β -oxidation of very long chain fatty acids. Importantly, in x-linked adrenoleukodystrophy (ALD), fatty acid metabolism is abnormal, due to defects in the peroxisomal ABC transporter. Any agent that upregulates ABC transporter expression or biological activity may therefore be useful for the treatment of ALD or any other lipid disorder.

ABC1 is expressed in macrophages and is required for engulfment of cells

undergoing programmed cell death. The apoptotic process itself, and its regulation, have important implications for disorders such as cancer, one mechanism of which is failure of cells to undergo cell death appropriately. ABC1 may facilitate apoptosis, and as such may represent an intervention point for cancer treatment. Increasing ABC1 expression or activity or otherwise up-regulating ABC1 by any method may constitute a treatment for cancer by increasing apoptosis and thus potentially decreasing the aberrant cellular proliferation characterized by this disease. Conversely, down-regulation of ABC1 by any method may provide opportunity for decreasing apoptosis and allowing increased proliferation of cells in conditions where cell growth is limited. Such disorders include but are not limited to neurodeficiencies and neurodegeneration, and growth disorders. ABC1 could, therefore, be used as a method for identification of compounds for use in the treatment of cancer, or in the treatment of degenerative disorders.

Agents that have been shown to inhibit ABC1 include, for example, the anti-diabetic agents glibenclamide and glyburide, flufenamic acid, diphenylamine-2-carbonic acid, sulfobromophthalein, and DIDS.

Agents that upregulate ABC1 expression or biological activity include but are not limited to protein kinase A, protein kinase C, vanadate, okadaic acid, and IBMX1.

biological activity.

There is evidence that, in addition to its role as a regulator of cholesterol levels, ABC1 also transports anions. Functional assays could be based upon this property, and could employ drug screening technology such as (but not
5 limited to) the ability of various dyes to change color in response to changes in specific ion concentrations in such assays can be performed in vesicles such as liposomes, or adapted to use whole cells.

Drug screening assays can also be based upon the ability of ABC1 or other ABC transporters to interact with other proteins. Such interacting
10 proteins can be identified by a variety of methods known in the art, including, for example, radioimmunoprecipitation, co-immunoprecipitation, co-purification, and yeast two-hybrid screening. Such interactions can be further assayed by means including but not limited to fluorescence polarization or scintillation proximity methods. Drug screens can also be based upon
15 functions of the ABC1 protein deduced upon X-ray crystallography of the protein and comparison of its 3-D structure to that of proteins with known functions. Such a crystal structure has been determined for the prokaryotic ABC family member HisP, histidine permease. Drug screens can be based upon a function or feature apparent upon creation of a transgenic or knockout
20 mouse, or upon overexpression of the protein or protein fragment in mammalian cells *in vitro*. Moreover, expression of mammalian (e.g., human) ABC1 in yeast or *C. elegans* allows for screening of candidate compounds in wild-type and mutant backgrounds, as well as screens for mutations that enhance or suppress an ABC1-dependent phenotype. Modifier screens can
25 also be performed in ABC1 transgenic or knock-out mice.

Additionally, drug screening assays can also be based upon ABC1 functions deduced upon antisense interference with the gene function. Intracellular localization of ABC1, or effects which occur upon a change in intracellular localization of the protein, can also be used as an assay for drug

screening. Immunocytochemical methods will be used to determine the exact location of the ABC1 protein.

Human and rodent ABC1 protein can be used as an antigen to raise antibodies, including monoclonal antibodies. Such antibodies will be useful for a wide variety of purposes, including but not limited to functional studies and the development of drug screening assays and diagnostics. Monitoring the influence of agents (e.g., drugs, compounds) on the expression or biological activity of ABC1 can be applied not only in basic drug screening, but also in clinical trials. For example, the effectiveness of an agent determined by a screening assay as described herein to increase ABC1 gene expression, protein levels, or biological activity can be monitored in clinical trials of subjects exhibiting altered ABC1 gene expression, protein levels, or biological activity. Alternatively, the effectiveness of an agent determined by a screening assay to modulate ABC1 gene expression, protein levels, or biological activity can be monitored in clinical trials of subjects exhibiting decreased altered gene expression, protein levels, or biological activity. In such clinical trials, the expression or activity of ABC1 and, preferably, other genes that have been implicated in, for example, cardiovascular disease can be used to ascertain the effectiveness of a particular drug.

For example, and not by way of limitation, genes, including ABC1, that are modulated in cells by treatment with an agent (e.g., compound, drug or small molecule) that modulates ABC1 biological activity (e.g., identified in a screening assay as described herein) can be identified. Thus, to study the effect of agents on cholesterol levels, triglyceride levels, or cardiovascular disease, for example, in a clinical trial, cells can be isolated and RNA prepared and analyzed for the levels of expression of ABC1 and other genes implicated in the disorder. The levels of gene expression can be quantified by Northern blot analysis or RT-PCR, or, alternatively, by measuring the amount of protein produced, by one of a number of methods known in the art, or by measuring

the levels of biological activity of ABC1 or other genes. In this way, the gene expression can serve as a marker, indicative of the physiological response of the cells to the agent. Accordingly, this response state may be determined before, and at various points during, treatment of the individual with the agent.

5 In a preferred embodiment, the present invention provides a method for monitoring the effectiveness of treatment of a subject with an agent (e.g., an agonist, antagonist, peptidomimetic, protein, peptide, nucleic acid, small molecule, or other drug candidate identified by the screening assays described herein) including the steps of (i) obtaining a pre-administration sample from a
10 subject prior to administration of the agent; (ii) detecting the level of expression of an ABC1 protein, mRNA, or genomic DNA in the preadministration sample; (iii) obtaining one or more post-administration samples from the subject; (iv) detecting the level of expression or activity of the ABC1 protein, mRNA, or genomic DNA in the post-administration
15 samples; (v) comparing the level of expression or activity of the ABC1 protein, mRNA, or genomic DNA in the pre-administration sample with the ABC1 protein, mRNA, or genomic DNA in the post administration sample or samples; and (vi) altering the administration of the agent to the subject accordingly. For example, increased administration of the agent may be
20 desirable to increase the expression or activity of ABC1 to higher levels than detected, i.e., to increase the effectiveness of the agent. Alternatively, decreased administration of the agent may be desirable to decrease expression or activity of ABC1 to lower levels than detected.

25 The *ABC1* gene or a fragment thereof can be used as a tool to express the protein in an appropriate cell *in vitro* or *in vivo* (gene therapy), or can be cloned into expression vectors which can be used to produce large enough amounts of ABC1 protein to use in *in vitro* assays for drug screening. Expression systems which may be employed include baculovirus, herpes virus, adenovirus, adeno-associated virus, bacterial systems, and eucaryotic systems

such as CHO cells. Naked DNA and DNA-liposome complexes can also be used.

Assays of ABC1 activity includes binding to intracellular interacting proteins; interaction with a protein that up-regulates ABC1 activity; interaction
5 with HDL particles or constituents; interaction with other proteins which facilitate interaction with HDL or its constituents; and measurement of cholesterol efflux. Furthermore, assays may be based upon the molecular dynamics of macromolecules, metabolites and ions by means of fluorescent-protein biosensors. Alternatively, the effect of candidate modulators on
10 expression or activity may be measured at the level of ABC1 protein production using the same general approach in combination with standard immunological detection techniques, such as Western blotting or immunoprecipitation with an ABC1-specific antibody. Again, useful cholesterol- or triglyceride-regulating or anti-CVD therapeutic modulators are
15 identified as those which produce an change in ABC1 polypeptide production. Agonists may also affect ABC1 activity without any effect on expression level.

Candidate modulators may be purified (or substantially purified) molecules or may be one component of a mixture of compounds (*e.g.*, an extract or supernatant obtained from cells). In a mixed compound assay,
20 ABC1 expression is tested against progressively smaller subsets of the candidate compound pool (*e.g.*, produced by standard purification techniques, *e.g.*, HPLC or FPLC; Ausubel *et al.*) until a single compound or minimal compound mixture is demonstrated to modulate ABC1 expression.

Agonists, antagonists, or mimetics found to be effective at modulating
25 the level of cellular ABC1 expression or activity may be confirmed as useful in animal models (for example, mice, pigs, rabbits, or chickens). For example, the compound may ameliorate the low HDL levels of mouse or chicken hypoalphalipoproteinemias or may lower the triglyceride levels in animal models.

A compound that promotes an increase in ABC1 expression or activity is considered particularly useful in the invention; such a molecule may be used, for example, as a therapeutic to increase the level or activity of native, cellular ABC1 and thereby treat a low HDL or high triglyceride condition in an animal (for example, a human). If desired, treatment with an agonist of the invention may be combined with any other HDL-raising, triglyceride-lowering, or anti-CVD therapies.

One method for increasing ABC biological activity is to increase the stabilization of the ABC protein or to prevent its degradation. Thus, it would be useful to identify mutations in an ABC polypeptide (e.g., ABC1) that lead to increased protein stability. These mutations can be incorporated into any protein therapy or gene therapy undertaken for the treatment of low HDL-C or any other condition resulting from loss of ABC1 biological activity. Similarly, compounds that increase the stability of a wild-type ABC polypeptide or decrease its catabolism may also be useful for the treatment of low HDL-C or any other condition resulting from loss of ABC1 biological activity. Such mutations and compounds can be identified using the methods described herein.

In one example, cells expressing an ABC polypeptide having a mutation are transiently metabolically labeled during translation and the half-life of the ABC polypeptide is determined using standard techniques. Mutations that increase the half-life of an ABC polypeptide are ones that increase ABC protein stability. These mutations can then be assessed for ABC biological activity. They can also be used to identify proteins that affect the stability of ABC1 mRNA or protein. One can then assay for compounds that act on these factors or on the ability of these factors to bind ABC1.

In another example, cells expressing wild-type ABC polypeptide are transiently metabolically labeled during translation, contacted with a candidate compounds, and the half-life of the ABC polypeptide is determined using

standard techniques. Compounds that increase the half-life of an ABC polypeptide are useful compounds in the present invention.

It is understood that, while ABC1 is the preferred ABC transporter for the drug screens described herein, other ABC transporters can also be used.

5 The replacement of ABC1 with another ABC transporter is possible because it is likely that ABC transporter family members, such as ABC2, ABCR, or ABC8 will have a similar mechanism of regulation.

Exemplary assays are described in greater detail below.

10 Protein-based assays

ABC1 polypeptide (purified or unpurified) can be used in an assay to determine its ability to bind another protein (including, but not limited to, proteins found to specifically interact with ABC1). The effect of a compound on that binding is then determined.

15

Protein Interaction Assays

ABC1 protein (or a polypeptide fragment thereof or an epitope-tagged form or fragment thereof) is harvested from a suitable source (e.g., from a prokaryotic expression system, eukaryotic cells, a cell-free system, or by immunoprecipitation from ABC1-expressing cells). The ABC1 polypeptide is then bound to a suitable support (e.g., nitrocellulose or an antibody or a metal agarose column in the case of, for example, a his-tagged form of ABC1). Binding to the support is preferably done under conditions that allow proteins associated with ABC1 polypeptide to remain associated with it. Such conditions may include use of buffers that minimize interference with protein-protein interactions. The binding step can be done in the presence and absence of compounds being tested for their ability to interfere with interactions between ABC1 and other molecules. If desired, other proteins (e.g., a cell lysate) are added, and allowed time to associate with the ABC

20

25

polypeptide. The immobilized ABC1 polypeptide is then washed to remove proteins or other cell constituents that may be non-specifically associated with it the polypeptide or the support. The immobilized ABC1 polypeptide is then dissociated from its support, and so that proteins bound to it are released (for example, by heating), or, alternatively, associated proteins are released from ABC1 without releasing the ABC1 polypeptide from the support. The released proteins and other cell constituents can be analyzed, for example, by SDS-PAGE gel electrophoresis, Western blotting and detection with specific antibodies, phosphoamino acid analysis, protease digestion, protein sequencing, or isoelectric focusing. Normal and mutant forms of ABC1 can be employed in these assays to gain additional information about which part of ABC1 a given factor is binding to. In addition, when incompletely purified polypeptide is employed, comparison of the normal and mutant forms of the protein can be used to help distinguish true binding proteins.

The foregoing assay can be performed using a purified or semipurified protein or other molecule that is known to interact with ABC1. This assay may include the following steps.

1. Harvest ABC1 protein and couple a suitable fluorescent label to it;
2. Label an interacting protein (or other molecule) with a second, different fluorescent label. Use dyes that will produce different quenching patterns when they are in close proximity to each other versus when they are physically separate (i.e., dyes that quench each other when they are close together but fluoresce when they are not in close proximity);
3. Expose the interacting molecule to the immobilized ABC1 in the presence or absence of a compound being tested for its ability to interfere with an interaction between the two; and
4. Collect fluorescent readout data.

Another assay is includes Fluorescent Resonance Energy Transfer (FRET) assay. This assay can be performed as follows.

1. Provide ABC1 protein or a suitable polypeptide fragment thereof and couple a suitable FRET donor (e.g., nitro-benzoxadiazole (NBD)) to it;
2. Label an interacting protein (or other molecule) with a FRET acceptor (e.g., rhodamine);
- 5 3. Expose the acceptor-labeled interacting molecule to the donor-labeled ABC1 in the presence or absence of a compound being tested for its ability to interfere with an interaction between the two; and
4. Measure fluorescence resonance energy transfer.

10 Quenching and FRET assays are related. Either one can be applied in a given case, depending on which pair of fluorophores is used in the assay.

Membrane permeability assay

15 The ABC1 protein can also be tested for its effects on membrane permeability. For example, beyond its putative ability to translocate lipids, ABC1 might affect the permeability of membranes to ions. Other related membrane proteins, most notably the cystic fibrosis transmembrane conductance regulator and the sulfonylurea receptor, are associated with and regulate ion channels.

20 ABC1 or a fragment of ABC1 is incorporated into a synthetic vesicle, or, alternatively, is expressed in a cell and vesicles or other cell sub-structures containing ABC1 are isolated. The ABC1-containing vesicles or cells are loaded with a reporter molecule (such as a fluorescent ion indicator whose fluorescent properties change when it binds a particular ion) that can detect ions (to observe outward movement), or alternatively, the external medium is
25 loaded with such a molecule (to observe inward movement). A molecule which exhibits differential properties when it is inside the vesicle compared to when it is outside the vesicle is preferred. For example, a molecule that has quenching properties when it is at high concentration but not when it is at another low concentration would be suitable. The movement of the charged

molecule (either its ability to move or the kinetics of its movement) in the presence or absence of a compound being tested for its ability to affect this process can be determined.

In another assay, membrane permeability is determined electro-physiologically by measuring ionic influx or efflux mediated by or modulated by ABC1 by standard electrophysiological techniques. A suitable control (e.g., TD cells or a cell line with very low endogenous ABC1 expression) can be used as a control in the assay to determine if the effect observed is specific to cells expressing ABC1.

In still another assay, uptake of radioactive isotopes into or out of a vesicle can be measured. The vesicles are separated from the extravesicular medium and the radioactivity in the vesicles and in the medium is quantitated and compared.

15. Nucleic acid-based assays

ABC1 nucleic acid may be used in an assay based on the binding of factors necessary for ABC1 gene transcription. The association between the ABC1 DNA and the binding factor may be assessed by means of any system that discriminates between protein-bound and non-protein-bound DNA (e.g., a gel retardation assay). The effect of a compound on the binding of a factor to ABC1 DNA is assessed by means of such an assay. In addition to *in vitro* binding assays, *in vivo* assays in which the regulatory regions of the ABC1 gene are linked to reporter genes can also be performed.

25. Assays measuring ABC1 stability

A cell-based or cell-free system can be used to screen for compounds based on their effect on the half-life of ABC1 mRNA or ABC1 protein. The assay may employ labeled mRNA or protein. Alternatively, ABC1 mRNA may be detected by means of specifically hybridizing probes or a quantitative PCR

assay. Protein can be quantitated, for example, by fluorescent antibody-based methods.

In vitro mRNA stability assay

- 5 1. Isolate or produce, by *in vitro* transcription, a suitable quantity of ABC1 mRNA;
2. Label the ABC1 mRNA;
3. Expose aliquots of the mRNA to a cell lysate in the presence or absence of a compound being tested for its ability to modulate ABC1 mRNA
- 10 stability; and
4. Assess intactness of the remaining mRNA at suitable time points.

In vitro protein stability assay

1. Express a suitable amount of ABC1 protein;
- 15 2. Label the protein;
3. Expose aliquots of the labeled protein to a cell lysate in the presence or absence of a compound being tested for its ability to modulate ABC1 protein stability; and
4. Assess intactness of the remaining protein at suitable time points

20

In vivo mRNA or protein stability assay

1. Incubate cells expressing ABC1 mRNA or protein with a tracer (radiolabeled ribonucleotide or radiolabeled amino acid, respectively) for a very brief time period (e.g., five minutes) in the presence or absence of a
- 25 compound being tested for its effect on mRNA or protein stability;
2. Incubate with unlabeled ribonucleotide or amino acid; and
3. Quantitate the ABC1 mRNA or protein radioactivity at time intervals beginning with the start of step 2 and extending to the time when the radioactivity in ABC1 mRNA or protein has declined by approximately 80%.

It is preferable to separate the intact or mostly intact mRNA or protein from its radioactive breakdown products by a means such as gel electrophoresis in order to quantitate the mRNA or protein.

5 Assays measuring inhibition of dominant negative activity

 Mutant ABC1 polypeptides are likely to have dominant negative activity (i.e., activity that interferes with wild-type ABC1 function). An assay for a compound that can interfere with such a mutant may be based on any method of quantitating normal ABC1 activity in the presence of the mutant.
10 For example, normal ABC1 facilitates cholesterol efflux, and a dominant negative mutant would interfere with this effect. The ability of a compound to counteract the effect of a dominant negative mutant may be based on cellular cholesterol efflux, or on any other normal activity of the wild-type ABC1 that was inhibitable by the mutant.

15

Assays measuring phosphorylation

 Glu89 in the wild-type chicken ABC1 polypeptide is likely to be part of a phosphorylation motif, and thus elimination of this phosphorylation motif by the E \Rightarrow K ABC1 mutation in the WHAM chicken (discussed further below)
20 may be responsible for reduced biological activity of WHAM chicken ABC1. Thus, compounds that modulate the phosphorylation state of ABC1 are likely to be clinically relevant modulators of human ABC1 activity.

 The effect of a compound on ABC1 phosphorylation can be assayed by methods that quantitate phosphates on proteins or that assess the
25 phosphorylation state of a specific residue of a ABC1. Such methods include but are not limited to ³²P labeling and immunoprecipitation, detection with antiphosphoamino acid antibodies (e.g., antiphosphoserine antibodies), phosphoamino acid analysis on 2-dimensional TLC plates, and protease digestion fingerprinting of proteins followed by detection of ³²P-labeled

fragments.

Assays measuring other post-translational modifications

5 The effect of a compound on the post-translational modification of ABC1 is based on any method capable of quantitating that particular modification. For example, effects of compounds on glycosylation may be assayed by treating ABC1 with glycosylase and quantitating the amount and nature of carbohydrate released.

Assays measuring ATP binding

10 The ability of ABC1 to bind ATP provides another assay to screen for compounds that affect ABC1. ATP binding can be quantitated as follows.

1. Provide ABC1 protein at an appropriate level of purity and reconstitute it in a lipid vesicle;
- 15 2. Expose the vesicle to a labeled but non-hydrolyzable ATP analog (such as gamma ³⁵S-ATP) in the presence or absence of compounds being tested for their effect on ATP binding. Note that azido-ATP analogs can be used to allow covalent attachment of the azido-ATP to protein (by means of U.V. light), and permit easier quantitation of the amount of ATP bound to the protein; and
- 20 3. Quantitate the amount of ATP analog associated with ABC1

Assays measuring ATPase activity

25 Quantitation of the ATPase activity of ABC1 can also be assayed for the effect of compounds on ABC1. This is preferably performed in a cell-free assay so as to separate ABC1 from the many other ATPases in the cell. An ATPase assay may be performed in the presence or absence of membranes, and with or without integration of ABC1 protein into a membrane. If performed in a vesicle-based assay, the ATP hydrolysis products produced or the ATP

hydrolyzed may be measured within or outside of the vesicles, or both. Such an assay may be based on disappearance of ATP or appearance of ATP hydrolysis products.

For high-throughput screening, a coupled ATPase assay is preferable. For example, a reaction mixture containing pyruvate kinase and lactate dehydrogenase can be used. The mixture includes phosphoenolpyruvate (PEP), nicotinamide adenine dinucleotide (NAD⁺), and ATP. The ATPase activity of ABC1 generates ADP from ATP. The ADP is then converted back to ATP as part of the pyruvate kinase reaction. The product, pyruvate, is then converted to lactate. The latter reaction generates a colored quinone (NADH) from a colorless substrate (NAD⁺), and the entire reaction can be monitored by detection of the color change upon formation of NADH. Since ADP is limiting for the pyruvate kinase reaction, this coupled system precisely monitors the ATPase activity of ABC1.

Assays measuring cholesterol efflux

A transport-based assay can be performed *in vivo* or *in vitro*. For example, the assay may be based on any part of the reverse cholesterol transport process that is readily re-created in culture, such as cholesterol or phospholipid efflux. Alternatively, the assay may be based on net cholesterol transport in a whole organism, as assessed by means of a labeled substance (such as cholesterol).

For high throughput, fluorescent lipids can be used to measure ABC1-catalyzed lipid efflux. For phospholipids, a fluorescent precursor, C6-NBD-phosphatidic acid, can be used. This lipid is taken up by cells and dephosphorylated by phosphatidic acid phosphohydrolase. The product, NBD-diglyceride, is then a precursor for synthesis of glycerophospholipids like phosphatidylcholine. The efflux of NBD-phosphatidylcholine can be monitored by detecting fluorescence resonance energy transfer (FRET) of the

NBD to a suitable acceptor in the cell culture medium. This acceptor can be rhodamine-labeled phosphatidylethanolamine, a phospholipid that is not readily taken up by cells. The use of short-chain precursors obviates the requirement for the phospholipid transfer protein in the media. For
5 cholesterol, NBD-cholesterol ester can be reconstituted into LDL. The LDL can efficiently deliver this lipid to cells via the LDL receptor pathway. The NBD-cholesterol esters are hydrolyzed in the lysosomes, resulting in NBD-cholesterol that can now be transported back to the plasma membrane and efflux from the cell. The efflux can be monitored by the aforementioned
10 FRET assay in which NBD transfers its fluorescence resonance energy to the rhodamine-phosphatidylethanolamine acceptor.

Animal Model Systems

Compounds identified as having activity in any of the above-described
15 assays are subsequently screened in any available animal model system, including, but not limited to, pigs, rabbits, and WHAM chickens. Test compounds are administered to these animals according to standard methods. Test compounds may also be tested in mice bearing mutations in the *ABC1* gene. Additionally, compounds may be screened for their ability to enhance an
20 interaction between ABC1 and any HDL particle constituent such as ApoAI, ApoAII, or ApoE.

The cholesterol efflux assay as a drug screen

The cholesterol efflux assay measures the ability of cells to transfer
25 cholesterol to an extracellular acceptor molecule and is dependent on ABC1 function. In this procedure, cells are loaded with radiolabeled cholesterol by any of several biochemical pathways (Marcil *et al.*, Arterioscler. Thromb. Vasc. Biol. 19:159-169, 1999). Cholesterol efflux is then measured after incubation for various times (typically 0 to 24 hours) in the presence of HDL3

or purified ApoAI. Cholesterol efflux is determined as the percentage of total cholesterol in the culture medium after various times of incubation. ABC1 expression levels and/or biological activity are associated with increased efflux while decreased levels of ABC1 are associated with decreased cholesterol efflux.

This assay can be readily adapted to the format used for drug screening, which may consist of a multi-well (*e.g.*, 96-well) format. Modification of the assay to optimize it for drug screening would include scaling down and streamlining the procedure, modifying the labeling method, using a different cholesterol acceptor, altering the incubation time, and changing the method of calculating cholesterol efflux. In all these cases, the cholesterol efflux assay remains conceptually the same, though experimental modifications may be made. A transgenic mouse overexpressing ABC1 would be expected to have higher than normal HDL levels.

Knock-out mouse model

An animal, such as a mouse, that has had one or both ABC1 alleles inactivated (*e.g.*, by homologous recombination) is likely to have low HDL-C levels and higher than normal triglyceride levels, and thus is a preferred animal model for screening for compounds that raise HDL-C levels or lower triglyceride levels. Such an animal can be produced using standard techniques. In addition to the initial screening of test compounds, the animals having mutant ABC1 genes are useful for further testing of efficacy and safety of drugs or agents first identified using one of the other screening methods described herein. Cells taken from the animal and placed in culture can also be exposed to test compounds. HDL-C and triglyceride levels can be measured using standard techniques, such as those described herein.

WHAM chickens: an animal model for low HDL cholesterol

Wisconsin Hypo-Alpha Mutant (WHAM) chickens arose by spontaneous mutation in a closed flock. Mutant chickens came to attention through their a Z-linked white shank and white beak phenotype referred to as
5 'recessive white skin' (McGibbon, 1981) and were subsequently found to have a profound deficiency of HDL (Poernama *et al.*, 1990).

This chicken low HDL locus (Y) is Z-linked, or sex-linked. (In birds, females are ZW and males are ZZ). Genetic mapping placed the Y locus on the long arm of the Z chromosome (Bitgood, 1985), proximal to the ID locus
10 (Bitgood, 1988). Examination of current public mapping data for the chicken genome mapping project, ChickMap (maintained by the Roslin Institute; <http://www.ri.bbsrc.ac.uk/chickmap/ChickMapHomePage.html>) showed that a region of synteny with human chromosome 9 lies on the long arm of the chicken Z chromosome (Zq) proximal to the ID locus. Evidence for this
15 region of synteny is the location of the chicken aldolase B locus (ALDOB) within this region. The human ALDOB locus maps to chromosome 9q22.3 (The Genome Database, <http://gdbwww.gdb.org/>), not far from the location of human ABC1. This comparison of maps showed that the chicken Zq region near chicken ALDOB and the human 9q region near human ALDOB represent
20 a region of synteny between human and chicken.

Since a low HDL locus maps to the 9q location in humans and to the Zq region in chickens, these low HDL loci are most probably located within the syntenic region. Thus we predicted that ABC1 is mutated in WHAM chickens. In support of this, we have previously identified an E⇒K mutation at a
25 position that corresponds to amino acid 89 of human ABC1. This non-conservative substitution is at a position that is conserved among human, mouse, and chicken, indicating that it is in a region of the protein likely to be of functional importance.

Discovery of the WHAM mutation in the amino-terminal portion of the ABC1 protein also establishes the importance of the amino-terminal region. This region may be critical because of association with other proteins required to carry out cholesterol efflux or related tasks. It may be an important regulatory region (there is a phosphorylation site for casein kinase near the mutated residue), or it may help to dictate a precise topological relationship with cellular membranes (the N-terminal 60 amino acid region contains a putative membrane-spanning or membrane-associated segment).

The amino-terminal region of the protein (up to the first 6-TM region at approximately amino acid 639) is an ideal tool for screening factors that affect ABC1 activity. It can be expressed as a truncated protein in ABC1 wild-type cells in order to test for interference of the normal ABC1 function by the truncated protein. If the fragment acts in a dominant negative way, it could be used in immunoprecipitations to identify proteins that it may be competing away from the normal endogenous protein.

The C-terminus also lends itself to such experiments, as do the intracellular portions of the molecule, expressed as fragments or tagged or fusion proteins, in the absence of transmembrane regions.

Since it is possible that there are several genes in the human genome which affect cholesterol efflux, it is important to establish that any animal model to be used for a human genetic disease represents the homologous locus in that animal, and not a different locus with a similar function. The evidence above establishes that the chicken Y locus and the human chromosome 9 low HDL locus are homologous. WHAM chickens are therefore an important animal model for the identification and testing of drugs that modulate cholesterol efflux.

The WHAM chickens' HDL deficiency syndrome is not, however, known to be associated with an increased susceptibility to atherosclerosis in chickens. This may reflect the shorter lifespan or, more likely, the impaired

absorption of dietary cholesterol in these chickens. We propose the WHAM chicken as a model for human low HDL for the development and testing of drugs to raise HDL in humans. Such a model could be employed in several forms, through the use of cells or other derivatives of these chickens, or by the use of the chickens themselves in tests of drug effectiveness, toxicity, and other drug development purposes.

Therapy

Compounds of the invention, including but not limited to, ABC1 polypeptides, *ABC1* nucleic acids, other ABC transporters, LXR-modulating compounds, RXR-modulating compounds, and any therapeutic agent that modulates biological activity or expression of ABC1 identified using any of the methods disclosed herein, may be administered with a pharmaceutically-acceptable diluent, carrier, or excipient, in unit dosage form. Conventional pharmaceutical practice may be employed to provide suitable formulations or compositions to administer such compositions to patients. Any appropriate route of administration may be employed, for example, intravenous, perenteral, subcutaneous, intramuscular, intracranial, intraorbital, ophthalmic, intraventricular, intracapsular, intraspinal, intracisternal, intraperitoneal, intranasal, aerosol, or oral administration. Therapeutic formulations may be in the form of liquid solutions or suspension; for oral administration, formulations may be in the form of tablets or capsules; and for intranasal formulations, in the form of powders, nasal drops, or aerosols.

Methods well known in the art for making formulations are found in, for example, Remington: The Science and Practice of Pharmacy, (19th ed.) ed. A.R. Gennaro AR., 1995, Mack Publishing Company, Easton, PA. Formulations for parenteral administration may, for example, contain excipients, sterile water, or saline, polyalkylene glycols such as polyethylene glycol, oils of vegetable origin, or hydrogenated naphthalenes. Biocompatible,

biodegradable lactide polymer, lactide/glycolide copolymer, or polyoxyethylene-polyoxypropylene copolymers may be used to control the release of the compounds. Other potentially useful parenteral delivery systems for agonists of the invention include ethylenevinyl acetate copolymer particles, osmotic pumps, implantable infusion systems, and liposomes. Formulations for inhalation may contain excipients, for example, lactose, or may be aqueous solutions containing, for example, polyoxyethylene-9-lauryl ether, glycocholate and deoxycholate, or may be oily solutions for administration in the form of nasal drops, or as a gel.

Compounds

In general, novel drugs for the treatment of aberrant lipid levels and/or CVD are identified from large libraries of both natural product or synthetic (or semi-synthetic) extracts or chemical libraries according to methods known in the art. Those skilled in the field of drug discovery and development will understand that the precise source of test extracts or compounds is not critical to the screening procedure(s) of the invention. Accordingly, virtually any number of chemical extracts or compounds can be screened using the exemplary methods described herein. Examples of such extracts or compounds include, but are not limited to, plant-, fungal-, prokaryotic- or animal-based extracts, fermentation broths, and synthetic compounds, as well as modification of existing compounds. Numerous methods are also available for generating random or directed synthesis (*e.g.*, semi-synthesis or total synthesis) of any number of chemical compounds, including, but not limited to, saccharide-, lipid-, peptide-, and nucleic acid-based compounds. Synthetic compound libraries are commercially available from Brandon Associates (Merrimack, NH) and Aldrich Chemical (Milwaukee, WI). Alternatively, libraries of natural compounds in the form of bacterial, fungal, plant, and animal extracts are commercially available from a number of sources,

including Biotics (Sussex, UK), Xenova (Slough, UK), Harbor Branch
Oceangraphics Institute (Ft. Pierce, FL), and PharmaMar, U.S.A. (Cambridge,
MA). In addition, natural and synthetically produced libraries are produced, if
desired, according to methods known in the art, *e.g.*, by standard extraction
5 and fractionation methods. Furthermore, if desired, any library or compound is
readily modified using standard chemical, physical, or biochemical methods.

In addition, those skilled in the art of drug discovery and development
readily understand that methods for dereplication (*e.g.*, taxonomic
dereplication, biological dereplication, and chemical dereplication, or any
10 combination thereof) or the elimination of replicates or repeats of materials
already known for their HDL-raising, triglyceride-lowering, or anti-CVD
activities, or known for their ability to modulate ABC1 gene expression or
ABC1 biological activity should be employed whenever possible.

When a crude extract is found to modulate ABC1 gene expression,
15 ABC1 biological activity, or a combination thereof, further fractionation of the
positive lead extract is necessary to isolate chemical constituent responsible for
the observed effect. Thus, the goal of the extraction, fractionation, and
purification process is the careful characterization and identification of a
chemical entity within the crude extract having HDL-raising, triglyceride-
20 lowering, or anti-CVD activities, ability to modulate ABC1 gene expression, or
a combination thereof. The same *in vivo* and *in vitro* assays described herein
for the detection of activities in mixtures of compounds can be used to purify
the active component and to test derivatives thereof. Methods of fractionation
and purification of such heterogeneous extracts are known in the art. If
25 desired, compounds shown to be useful agents for the treatment of
pathogenicity are chemically modified according to methods known in the art.
Compounds identified as being of therapeutic value are subsequently analyzed
using any standard animal model of diabetes or obesity known in the art.

It is understood that compounds that modulate activity of proteins that modulate ABC1 gene expression or activity are useful compounds for modulating HDL-C levels and triglyceride levels. Exemplary compounds are provided herein; others are known in the art.

5 Compounds that are structurally related to cholesterol, or that mimic ApoAI or a related apolipoprotein, and increase ABC1 biological activity are particularly useful compounds in the invention. Other compounds, known to act on the MDR protein, can also be used or derivatized and assayed for their ability to increase ABC1 biological activity. Exemplary MDR modulators are
10 PSC833, bromocriptine, and cyclosporin A. Other examples of compounds that may be assayed for the ability to increase ABC1 biological activity include oxysterols and their derivatives.

Screening patients having low HDL-C or high triglyceride levels

15 ABC1 expression, biological activity, and mutational analysis can each serve as a diagnostic tool for low HDL or higher than normal triglyceride levels; thus determination of the genetic subtyping of the *ABC1* gene sequence can be used to subtype low HDL or higher than normal triglyceride individuals or families to determine whether the low HDL or higher than normal
20 triglyceride phenotype is related to ABC1 function. This diagnostic process can lead to the tailoring of drug treatments according to patient genotype, including prediction of side-effects upon administration of HDL increasing or triglyceride lowering drugs (referred to herein as pharmacogenomics). Pharmacogenomics allows for the selection of agents (e.g., drugs) for
25 therapeutic or prophylactic treatment of an individual based on the genotype of the individual (e.g., the genotype of the individual is examined to determine the ability of the individual to respond to a particular agent).

Agents, or modulators which have a stimulatory or inhibitory effect on ABC1 biological activity or gene expression can be administered to individuals to treat disorders (e.g., cardiovascular disease, low HDL cholesterol, or a higher than normal triglyceride level) associated with aberrant ABC1 activity.

5 In conjunction with such treatment, the pharmacogenomics (i.e., the study of the relationship between an individual's genotype and that individual's response to a foreign compound or drug) of the individual may be considered. Differences in efficacy of therapeutics can lead to severe toxicity or therapeutic failure by altering the relation between dose and blood concentration of the pharmacologically active drug. Thus, the pharmacogenomics of the individual

10 permits the selection of effective agents (e.g., drugs) for prophylactic or therapeutic treatments based on a consideration of the individual's genotype. Such pharmacogenomics can further be used to determine appropriate dosages and therapeutic regimens. Accordingly, the activity of ABC1 protein, expression of ABC1 nucleic acid, or mutation content of ABC1 genes in an

15 individual can be determined to thereby select appropriate agent(s) for therapeutic or prophylactic treatment of the individual.

Pharmacogenomics deals with clinically significant hereditary variations in the response to drugs due to altered drug disposition and abnormal action in affected persons (Eichelbaum, M., Clin. Exp. Pharmacol. Physiol., 23:983-985,

20 1996; Linder, M. W., Clin. Chem., 43:254-266, 1997). In general, two types of pharmacogenetic conditions can be differentiated. Genetic conditions transmitted as a single factor altering the way drugs act on the body (altered drug action) or genetic conditions transmitted as single factors altering the way

25 the body acts on drugs (altered drug metabolism). Altered drug action may occur in a patient having a polymorphism (e.g., an single nucleotide polymorphism or SNP) in promoter, intronic, or exonic sequences of ABC1. Thus by determining the presence and prevalence of polymorphisms allow for prediction of a patient's response to a particular therapeutic agent. In

particular, polymorphisms in the promoter region may be critical in determining the risk of HDL deficiency, higher than normal triglyceride level, and CVD.

5 In addition to the mutations in the *ABCI* gene described herein, we have detected polymorphisms in the human *ABCI* gene (Fig. 4). These polymorphisms are located in promoter, intronic, and exonic sequence of *ABCI*. Using standard methods, such as direct sequencing, PCR, SSCP, or any other polymorphism-detection system, one could easily ascertain whether these polymorphisms are present in a patient prior to the establishment of a
10 drug treatment regimen for a patient having low HDL, a higher than normal triglyceride level, cardiovascular disease, or any other *ABCI*-mediated condition. It is possible that some these polymorphisms are, in fact, weak mutations. Individuals harboring such mutations may have an increased risk for cardiovascular disease; thus, these polymorphisms may also be useful in
15 diagnostic assays.

Other Embodiments

All publications mentioned in this specification are herein incorporated by reference to the same extent as if each independent publication was
20 specifically and individually indicated to be incorporated by reference.

While the invention has been described in connection with specific embodiments thereof, it will be understood that it is capable of further modifications. This application is intended to cover any variations, uses, or adaptations following, in general, the principles of the invention and including
25 such departures from the present disclosure within known or customary practice within the art to which the invention pertains and may be applied to the essential features hereinbefore set forth.

What is claimed is:

1. A method for treating a patient diagnosed as having a lower than normal HDL-cholesterol level, a higher than normal triglyceride level, or a cardiovascular disease, said method comprising administering to said patient a compound that modulates LXR-mediated transcriptional activity.

5

2. The method of claim 1, wherein said compound is an oxysterol.

3. The method of claim 1, wherein said compound is selected from the group consisting of 24-(S),25-epoxycholesterol; 24(S)-hydroxycholesterol;
10 22-(R)-hydroxycholesterol; 24(R),25-epoxycholesterol;
22(R)-hydroxy-24(S),25-epoxycholesterol;
22(S)-hydroxy-24(R),25-epoxycholesterol; 24-(S),25-iminocholesterol;
methyl-38-hydroxychololate; N,N-dimethyl-3 β -hydroxychololateamide;
24(R)-hydroxycholesterol; 22(S)-hydroxycholesterol;
15 22(R),24(S)-dihydroxycholesterol; 25-hydroxycholesterol;
22(R)-hydroxycholesterol; 22(S)-hydroxycholesterol;
24(S),25-dihydroxycholesterol; 24(R),25-dihydroxycholesterol;
24,25-dehydrocholesterol; 25-epoxy-22(R)-hydroxycholesterol;
20 20(S)-hydroxycholesterol; (20R,22R)-cholest-5-ene-3 β ,20,22-triol;
4,4-dimethyl-5- α -cholesta-8,14,24-trien-3- β -ol;
7 α -hydroxy-24(S),25-epoxycholesterol;
7 β -hydroxy-24(S),25-epoxycholesterol; 7-oxo-24(S),25-epoxycholesterol;
7 α -hydroxycholesterol; 7-oxocholesterol;
and desmosterol.

25

4. The method of claim 1, wherein said LXR is LXRA.

5. A method for treating a patient diagnosed as having a lower than normal HDL-cholesterol level, a higher than normal triglyceride level, or a cardiovascular disease, said method comprising administering to said patient a compound that modulates RXR-mediated transcriptional activity.

5

6. The method of claim 5, wherein said RXR is RXR α .

7. A method for determining whether a candidate compound modulates ABC1 expression, said method comprising the steps of:

10

(a) providing a nucleic acid molecule comprising an ABC1 regulatory region or promoter linked to a reporter gene;

(b) contacting said nucleic acid molecule with said candidate compound; and

(c) measuring expression of said reporter gene,

15

wherein altered reporter gene expression, relative to said reporter gene expression of a corresponding control nucleic acid molecule not contacted with said compound, indicates that said candidate compound modulates ABC1 expression.

20

8. The method of claim 7, wherein said regulatory region comprises 50 consecutive nucleotides selected from nucleotides 5854 to 6694, 7756 to 8318, 10479 to 10825, 15214 to 16068, 21636 to 22111, 27898 to 28721, 32951 to 33743, 36065 to 36847, 39730 to 40577, 4543 to 5287, and 45081 to 55639 of SEQ ID NO: 1.

25

9. The method of claim 7, wherein said regulatory region comprises a binding site for a transcription factor selected from a group consisting of LXRs, RXRs, RORs, SREBPs, and PPARs.

10. A substantially pure nucleic acid molecule comprising a region that is substantially identical to at least fifty contiguous nucleotides of nucleotides 5854 to 6694, 7756 to 8318, 10479 to 10825, 15214 to 16068, 21636 to 22111, 27898 to 28721, 32951 to 33743, 36065 to 36847, 39730 to 40577,
5 4543 to 5287, or 45081 to 55639 of SEQ ID NO: 1.

11. A substantially pure nucleic acid molecule comprising a region that is substantially identical to nucleotides 1 to 28,707 of SEQ ID NO: 1.

10 12. A substantially pure nucleic acid molecule comprising a region that is substantially identical to nucleotides 29,011 to 53,228 of SEQ ID NO: 1.

13. A cell expressing the nucleic acid molecule of claim 10.

15 14. A non-human mammal expressing the nucleic acid molecule of claim 10.

15. A method of treating a human having a higher than normal triglyceride level, said method comprising administering to said human an
20 ABC1 polypeptide, or triglyceride-regulating fragment thereof.

16. The method of claim 15, wherein said ABC1 polypeptide has the sequence of SEQ ID NO: 5.

25 17. The method of claim 15, wherein said ABC1 polypeptide comprises a R⇒K mutation at position 219 or a V⇒A mutation at position 399.

18. The method of claim 15, wherein said ABC1 polypeptide comprises a mutation that increases its stability.

19. The method of claim 15, wherein said ABC1 polypeptide comprises a mutation that increases its biological activity.

5 20. A method of treating a human having a higher than normal triglyceride level, said method comprising administering to said human a nucleic acid molecule encoding an ABC1 polypeptide or a triglyceride-regulating fragment thereof.

10 21. The method of claim 20, wherein said ABC1 polypeptide has the amino acid sequence of SEQ ID NO: 5.

22. The method of claim 20, wherein said ABC1 polypeptide comprises a R⇒K mutation at position 219 or a V⇒A mutation at position 399.

15 23. The method of claim 20, wherein said ABC1 polypeptide comprises a mutation that increases its stability.

24. The method of claim 20, wherein said ABC1 polypeptide comprises a mutation that increases its biological activity.

20

25. The method of claim 20, wherein said biological activity is regulation of cholesterol.

25 26. The method of claim 20, wherein said human has a lower than normal HDL-cholesterol level.

27. A method of treating a human having a higher than normal triglyceride level, said method comprising administering to said human a compound that increases ABC1 biological activity or that mimics the activity of wild-type ABC1, R219K ABC1, or V399A ABC1.

28. A non-human mammal comprising a transgene comprising a nucleic acid molecule encoding a dominant-negative ABC1 polypeptide, said dominant-negative polypeptide comprising a M \Rightarrow T mutation at position 1091.

29. A method for determining whether a candidate compound decreases the inhibition of a dominant-negative ABC1 polypeptide, said dominant-negative polypeptide comprising a M \Rightarrow T mutation at position 1091, said method comprising the steps of:

- (a) providing a cell expressing a dominant-negative ABC1 polypeptide;
- (b) contacting said cell with said candidate compound; and
- (c) measuring ABC1 biological activity of said cell,

wherein an increase in said ABC1 biological activity, relative to said ABC1 biological activity in a corresponding control cell not contacted with said compound, indicates that said candidate compound decreases the inhibition of a dominant-negative ABC1 polypeptide.

30. A method for predicting a person's response to a triglyceride-lowering drug, comprising determining whether the person has a polymorphism in an ABC1 gene, promoter, or regulatory sequence that alters the person's response to said drug.

31. A method for determining whether a candidate compound is useful for modulating triglyceride levels, said method comprising the steps of:

- (a) providing a chicken comprising a mutation in an *ABC1* gene;
- (b) administering said candidate compound to said chicken; and

5 (c) measuring ABC1 biological activity in said chicken,
wherein altered ABC1 biological activity, relative to said ABC1 biological activity in a corresponding control chicken not contacted with said compound, indicates that said candidate compound is useful for modulating triglyceride levels.

10

32. The method of claim 31, wherein said ABC1 biological activity is transport of cholesterol.

33. A method for determining whether a candidate compound is useful
15 for modulating triglyceride levels, said method comprising the steps of:

- (a) providing a cell expressing an ABC1 polypeptide comprising amino acids 1 to 60 of SEQ ID NO: 5;

- (b) contacting said cell with said candidate compound; and

- (c) measuring ABC1 biological activity of said cell,

20 wherein altered ABC1 biological activity, relative to said ABC1 biological activity in a corresponding control cell not contacted with said compound, indicates that said candidate compound is useful for modulating triglyceride levels.

25

34. A method for determining whether a candidate compound is useful for modulating triglyceride levels, said method comprising the steps of:

- (a) providing a cell expressing an *ABC1* gene or a fragment thereof;
- (b) contacting said cell with said candidate compound; and
- 5 (c) measuring ABC1 expression of said cell,

wherein altered ABC1 expression, relative to said ABC1 expression in a corresponding control cell not contacted with said candidate compound, indicates that said candidate compound is useful for modulating triglyceride levels.

10

35. A method for determining whether a candidate compound is useful for modulating triglyceride levels, said method comprising the steps of:

- (a) providing an ABC1 polypeptide comprising amino acids 1 to 60 of SEQ ID NO: 1;

15

- (b) contacting said polypeptide with said candidate compound; and

- (c) measuring ABC1 biological activity, wherein a change in ABC1 biological activity, relative to said ABC1 biological activity of a corresponding control ABC1 polypeptide not contacted with said compound, indicates that said candidate compound is useful for modulating triglyceride levels.

20

36. A method for determining whether a candidate compound is useful for modulating triglyceride levels, said method comprising the steps of:

(a) providing an ABC1 polypeptide comprising amino acids 1 to 60 of SEQ ID NO: 5;

5 (b) contacting said polypeptide with said candidate compound; and

(c) measuring expression of said ABC1 polypeptide,

wherein a change in expression of said ABC1 polypeptide, relative to said expression of a corresponding control ABC1 polypeptide not contacted with said compound, indicates that said candidate compound is useful for

10 modulating triglyceride levels.

37. A method for determining whether candidate compound is useful for modulating triglyceride levels, said method comprising the steps of:

15 (a) providing an ABC1 polypeptide comprising amino acids 1 to 60 of SEQ ID NO: 5;

(b) contacting said polypeptide with said candidate compound; and

(c) measuring binding of said ABC1 polypeptide to said candidate compound, wherein binding of said ABC1 polypeptide to said compound indicates that said candidate compound is useful for modulating triglyceride
20 levels.

38. A method for determining whether candidate compound is useful for modulating triglyceride levels, said method comprising the steps of:

(a) providing (i) an ABC1 polypeptide comprising amino acids 1 to 60 of SEQ ID NO: 5, and (ii) a second polypeptide that interacts with said ABC1 polypeptide;

(b) contacting said polypeptides with said candidate compound; and

(c) measuring interaction of said ABC1 polypeptide with said second polypeptide, wherein an alteration in the interaction of said ABC1 polypeptide with said second polypeptide indicates that said candidate compound is useful for modulating triglyceride levels.

39. A method for determining whether a candidate compound is useful for modulating triglyceride levels, said method comprising the steps of:

(a) providing a cell comprising an ABC1 polypeptide comprising amino acids 1 to 60 of SEQ ID NO: 5;

(b) contacting said cell with said candidate compound; and

(c) measuring the half-life of said ABC1 polypeptide, wherein an increase in said half-life, relative to said half-life in a corresponding control cell not contacted with said compound, indicates that said candidate compound is useful for modulating triglyceride levels.

40. A method for determining whether a candidate compound is useful for modulating triglyceride levels, said method comprising the steps of:

- (a) providing an ABC1 polypeptide in a lipid membrane;
- (b) contacting said polypeptide with said candidate compound; and
- 5 (c) measuring ABC1-mediated lipid transport across said lipid membrane,

wherein a change in lipid transport, relative to said lipid transport of a corresponding control ABC1 polypeptide not contacted with said compound, indicates that said candidate compound is useful for modulating triglyceride

10 levels.

41. The method of claim 35-38, or 40, wherein said ABC1 polypeptide is in a cell-free system.

15 42. The method of claim 35-38, or 40, wherein said ABC1 polypeptide is in a cell.

43. The method of claim 42, wherein said cell is from a WHAM chicken.

20

44. The method of claim 42, wherein said cell is in a human or in a non-human mammal.

45. The method of claim 44, wherein said animal is a WHAM chicken.

25

46. The method of claim 31, 33, or 35, wherein said biological activity is transport of lipid or interleukin-1.

47. The method of claim 46, wherein said lipid is cholesterol.

48. The method of claim 47, wherein said cholesterol is HDL-cholesterol.

5 49. The method of claim 31, 33, or 35, wherein said biological activity is binding or hydrolysis of ATP by the ABC1 polypeptide.

10 50. A method of determining a propensity for a disease or condition in a subject, wherein said disease or condition is selected from the group consisting of a lower than normal HDL level, a higher than normal triglyceride level, and a cardiovascular disease, said method comprising determining the presence or absence of at least one ABC1 polymorphism in the polynucleotide sequence of an ABC1 regulatory region, promoter, or coding sequence or in the amino acid sequence of an ABC1 protein in a sample obtained from said subject, wherein the presence or absence of said ABC1 polymorphism is
15 indicative of a risk for said disease or condition.

20 51. The method of claim 50, further comprising analyzing at least five ABC1 polymorphic sites in said polynucleotide sequence or said amino acid sequence.

52. A method for determining whether an ABC1 polymorphism is indicative of a risk for a disease or condition in a subject, wherein said disease or condition is selected from the group consisting of a lower than normal HDL level, a higher than normal triglyceride level, and a cardiovascular disease, said method comprising the steps of:

(a) determining whether the prevalence of said disease or condition in a first subject or set of subjects differs from said prevalence of said disease or condition in a second subject or set of subjects;

(b) analyzing the polynucleotide sequence of an ABC1 regulatory region, promoter, or coding sequence or the amino acid sequence of an ABC1 protein in a sample obtained from said first subject or set of subjects and said second subject or set of subjects; and

(c) determining whether at least one ABC1 polymorphism differs between said first subject or set of subjects and said second subject or set of subjects, wherein the presence or absence of said ABC1 polymorphism is correlated with said prevalence of said disease or condition, thereby determining whether said ABC1 polymorphism is indicative of said risk.

53. The method of claim 52, further comprising analyzing at least five ABC1 polymorphic sites in said polynucleotide sequence or said amino acid sequence.

54. An electronic database comprising a plurality of sequence records of ABC1 polymorphisms correlated to records of predisposition to or prevalence of a disease or condition selected from the group consisting of a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease.

55. A method for selecting a preferred therapy for modulating ABC1 activity or expression in a subject, said method comprising:

(a) determining the presence or absence of at least one ABC1 polymorphism in the polynucleotide sequence of an ABC1 regulatory region, promoter, or coding sequence or in the amino acid sequence of an ABC1 protein in a sample obtained from said subject, wherein the presence or absence of said ABC1 polymorphism is indicative of the safety or efficacy of at least one therapy for modulating ABC1 expression or activity; and

(b) determining a preferred therapy for modulating ABC1 expression or activity in said subject.

56. The method of claim 55, further comprising analyzing at least five ABC1 polymorphic sites in said polynucleotide sequence or said amino acid sequence.

57. A method for determining whether a candidate compound is useful for the treatment of a disease or condition selected from the group consisting of a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease; said method comprising the steps of:

(a) providing an assay system having a measurable ABC1 biological activity;

(b) contacting said assay system with said candidate compound; and

(c) measuring ABC1 biological activity or ABC1 phosphorylation, wherein modulation of ABC1 biological activity or ABC1 phosphorylation, relative to said ABC1 biological activity or ABC1 phosphorylation in a corresponding control assay system not contacted with said candidate compound, indicates that said candidate compound is useful for the treatment of said disease or condition.

58. The method of claim 57, wherein said assay system is a cell based system

5 59. The method of claim 57, wherein said assay system is a cell free system.

60. A method for identifying a compound to be tested for an ability to ameliorate a disease or condition selected from the group consisting of a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease, said method comprising the steps of:

- 10 (a) contacting a subject or cell with a candidate compound;
- (b) measuring ABC1 expression, activity, or protein phosphorylation in said subject or cell; wherein altered ABC1 expression, activity, or protein phosphorylation; relative to said ABC1 expression, activity, or protein phosphorylation in a corresponding control subject or cell not contacted with
- 15 said candidate compound; identifies said candidate compound as a compound to be tested for an ability to ameliorate said disease or condition.

61. The method of claim 57 or 60, wherein said candidate compound

20 modulates said ABC1 protein phosphorylation and said ABC1 activity.

62. A method for determining whether a candidate compound is useful for modulating a disease or condition selected from the group consisting of a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease, said method comprising the steps of:

- 5 (a) providing a cell expressing an ABC1 gene or a fragment thereof;
- (b) contacting said cell with said candidate compound; and
- (c) measuring ABC1 activity of said cell, wherein altered ABC1 activity, relative to said ABC1 activity in a corresponding control cell not contacted with said compound, indicates that said candidate compound is
- 10 useful for modulating said disease or condition.

63. A method for determining whether a candidate compound is useful for modulating a disease or condition selected from the group consisting of a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease, said method comprising the steps of:

- 15 (a) contacting a cell expressing an ABC1 protein with said candidate compound;
- (b) measuring the phosphorylation of said ABC1 protein; wherein altered ABC1 protein phosphorylation, relative to said ABC1 protein phosphorylation in a corresponding control cell not contacted with said
- 20 candidate compound, indicates that said is useful for modulating said disease or condition.

64. A compound useful for the treatment of a disease or condition selected from the group consisting of a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease, wherein said compound modulates ABC1 biological activity, and wherein said compound is identified by the steps of:

(a) providing an assay system having a measurable ABC1 biological activity;

(b) contacting said assay system with said compound; and

(c) measuring ABC1 biological activity, wherein modulation of ABC1 biological activity, relative to said ABC1 biological activity in a corresponding control assay system not contacted with said compound, indicates that said compound is useful for the treatment of said disease or condition.

65. A compound useful for the treatment of a disease or condition selected from the group consisting of a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease, wherein said compound induces a change in ABC1 biological activity that mimics the change in ABC1 biological activity induced by the R219K ABC1 mutation.

66. A compound useful for the treatment of a disease or condition selected from the group consisting of a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease, wherein said compound binds or interacts with residue R219 of ABC1, thereby mimicking the change in ABC1 activity induced by the R219K ABC1 mutation.

67. A compound useful for the treatment of a disease or condition selected from the group consisting of a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease, wherein said compound induces a change in ABC1 biological activity that
5 mimics the change in ABC1 biological activity induced by the V339A ABC1 mutation.

68. A compound useful for the treatment of a disease or condition selected from the group consisting of a lower than normal HDL cholesterol
10 level, a higher than normal triglyceride level, and a cardiovascular disease, wherein said compound binds or interacts with residue V399 of ABC1, thereby mimicking the change in ABC1 activity induced by the V399A ABC1 mutation.

69. A compound that modulates ABC1 activity and binds or interacts
15 with an amino acid of ABC1, wherein said amino acid is a residue selected from amino acids 119 to 319 of ABC1 (SEQ ID NO: 5) or amino acids 299 to 499 of ABC1 (SEQ ID NO: 5).

20

70. A method for determining whether a candidate compound is useful for the treatment a disease or condition selected from the group consisting of a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease, said method comprising the steps of:

- 5 (a) providing an assay system having a measurable LXR biological activity;
- (b) contacting the assay system with said candidate compound; and
- (c) measuring LXR biological activity, wherein modulation of LXR biological activity, relative to said LXR biological activity in a corresponding control assay system not contacted with said candidate compound, indicates
- 10 that said candidate compound is useful for the treatment of said disease or condition.

71. A method for determining whether a candidate compound is useful for modulating ABC1 biological activity, said method comprising the steps of:

- 15 (a) providing an assay system having a measurable LXR biological activity;
- (b) contacting said assay system with said candidate compound; and
- (c) measuring LXR biological activity, wherein modulation of LXR biological activity, relative to said LXR biological activity in a corresponding control assay system not contacted with said candidate compound, indicates
- 20 that said candidate compound is useful for modulating ABC1 biological activity.

25 72. The method of claim 71, wherein said LXR biological activity is modulation of ABC1 expression.

73. A method for identifying a compound to be tested for an ability to modulate ABC1 biological activity, said method comprising the steps of:

(a) contacting a subject or cell with a candidate compound;

(b) assaying the activity of the LXR gene product in said subject or cell;

5 wherein modulation of said activity, relative to said activity in a corresponding control subject or cell not contacted with said candidate compound, identifies said candidate compound as a compound to be tested for an ability to modulate the biological activity of ABC1.

10 74. Use of an LXR gene product in an assay to identify compounds useful for the treatment of a disease or condition selected from the group consisting of a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease.

15 75. Use of a compound that modulates the activity or expression of an LXR gene product for the treatment of a disease or condition selected from the group consisting of a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease.

20

76. A method for identifying a compound to be tested for an ability to treat a disease or condition selected from the group consisting of a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease, said method comprising the steps of:

- 5 (a) providing an assay system having a measurable LXR biological activity;
- (b) contacting said assay system with the candidate compound; and
- (c) measuring LXR biological activity, wherein modulation of said LXR biological activity, relative to said LXR biological activity in a corresponding
- 10 control assay system not contacted with said candidate compound, identifies said candidate compound as a compound to be tested for an ability to treat said disease or condition.

77. A method for screening an candidate LXR agonist for the ability to treat a disease or condition selected from the group consisting of a lower than

15 normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease, said method comprising the steps of:

- (a) contacting said a with said candidate LXR agonist; and
- (b) measuring cholesterol efflux activity of said cell, wherein an
- 20 increase in said cholesterol efflux activity in said cell, relative to said cholesterol efflux in a corresponding control cell not contacted with said candidate LXR agonist, indicates that said candidate LXR agonist is useful for treating said disease or condition.

25

78. A method for screening a candidate LXR modulating compound for the ability to treat a disease or condition selected from the group consisting of a lower than normal HDL cholesterol level, a higher than normal triglyceride level, and a cardiovascular disease, said method comprising the steps of:

5 (a) contacting a cell with said candidate LXR modulating compound;
and

(b) measuring ABC1 biological activity of said cell; wherein an increase in ABC1 biological activity in said cell, relative to said ABC1 biological activity in a corresponding control cell not contacted with said LXR
10 modulating compound, indicates that said LXR modulating compound is useful for treating said disease or condition.

79. The method of any one of claims 71-78, wherein said cell or assay system comprises an exogenously supplied copy of an LXRE selected from the
15 group consisting of SEQ ID NO: 94, SEQ ID NO: 92, and the LXRE consensus motif at nucleotide -7670 of the 3' end of intron 1.

20

Figure 1

SEQ ID No: 2

gtctataatggcatgccacagggctctaaaactttgcagttttatcattaactcaaagtgaatgtatcatg
ccgctgactcaacattttgagagacaacaaatacaatgaatatcaagatacatatatataatgtattt
ctttttgagatggagtttccactgtttgtgtgtccaggtggagtacaatagcacgactcttggctcactgcaacc
tctgctcccccaggttcaagcaattgtcctgcctcagcctcccaagtagctaggattacagggcatgtgccacc
acacctggctaattttgtattttttaagtagagatgggggtttcaccatgttggtcaggctggctcgaactc
ctgacctcaggtgatccacctgcctcagcatctcaaaagtgtgggttacaggtgtgagccacccccacccgg
ccatatatatatattttgagatggagcttactctgtcaccacaggtggagtgcaatggcttgatctcggc
tcattgcaacctctgcctcccatgttcagatgattctcctgcctcagcctctcaagaagctgggttacagg
tgcatgccaccatgccccactaatttttatatttcatcatgtgggtttcaccatgttggccaggggtgggtgtcg
aactcctgacctcaagtgtatctgcctgccttcggcctcccaagtgctgggttacccggcatgaaccaatac
gcttggcaatattttttaagaaaaaaaatttcagggtgcaacagcatccaaaaagtaaccaatgatttta
gggtgaaggggtgaagacaaatgtaaactctttttttttttgaaatggcgtcttgcctctgcctaggct
ggagtgcattgggtgcaattgctgacttctgaagaccgaacatttttagtcaatttcaaacacaaatgtggaataa
ctcccgagtagctgggtattataggctcgcgcgcgcacgccccgctaattttgtgttttttagtagagacggg
gtttcaccatgttggccaggtgtgtctcaactcttgacttcaagtgtatccgctgccttggcctcccaag
tgctgggttacaggttgagccacccgggtgaaatgttaaattgttaaactgtgtttttgaaatgtcaatg
tataggataagggagaattgacttcttgaagaccgaacatttttagtcaatttcaaacacaaatgtggaataa
ttgtataaaacaggttcccttatcctgatgaggataagaatagtagtcttgcagatggaatgcccattcag
ctgtactttctagtgggttacgcccatagtagcactgttgatggaaccaggtatctgactttaggaaagatgt
tccccaaactggagctgacccagaggagcctgaccaacttggggaaagttaaagatctcatcacgtggagaa
taggggaaggacccaacagctattgagtgctactttgagccttaaggagagaaggagaaaaaggcagggaataa
acggaggtagggaataagaataggtaattcttctagggttaaataaataagtgcttgccataggaaggagccc
cagaacacagttatcaataatagagactcacacagagcattctacactagagctgctgtcctcttgaccaga
ataagggtgaaggtgtgtgtgtgtgtccaggaagtaggcagctaggaggtgatcagagcatcacactatgcc
ggcacaattctaaagtgtcttccctaggggaaatcctatttcttctcaggcacatttgtttattcttctatg
ttcactcttgttatttacttcttgcaggtcttgcgttaagaattggggaaacaagggttgaaataaaccaggt
ctgtaaaagaaaaggagctcacagctctggaggggcaaatgggcattgtgcctgcaagttggcccactgagagc
ctaagaagtgaagttatgaatccaggattactcagttatcaatgaagtgtatgaacatcatccatacagacc
ttcagagctggaggggaattttggatacctactcagcacatagttttcaaacagtgcttgtggaacccctagg
gcattttcttagggattgtgtgtgtgtgagagaggagattgaatcagaaggtgtctgggaccattctctactca
cacttcaagcagagcagctccacttctatctgtattattttttattttattttattttattttttga
gacggagctctgcctgtgcgccaggtggagtgagtgccacgatctcagctcactgcaacctctgcctcc
cgggttcaagagatttctcctgcctcagcctcctgagtagctggaattataggcctatgccaccacgcccagc
taatttttgtatttttagtagagacgggggtttcaccatgttggtcaggctggctcgaactcctgacctgtg
gatccaccggccttgcctcccaagtgctgggttacaggcattagccacctagccccgcctatctgtatt
atttattcattattgtctatgtgaatgaacctgaagaatgcttactgttactgtctaagttttaaccacaccc
catgcccattgcaggatgatagtgaaatagtgccaaaagataactataattagactcatgtaattaaaggaatat
ttttgtcttgtacctattatgtgcctataaagactatgaatctattttattcagtgattttattggaatacca
aataagcaagatcctatgtgctaaagattctaataattgtgctaagattttccttcagatgtttggctttct
caaattccctgagggttagaactttgcccactcatttgtgtttcccaagtgcttaacgcagtgctgacac
atacaggatctccaaacgcttgcctgaatgtgtgaggaaggaattaaaataatgtaccgcccgggcaagtggc
tcatgcctataatcccagcactttgagagaccgaggtgggcagatcacttgaggtcaggagctcagagcccag
cctggccaacatgggtgaaaccccgctctctactaagaatacaaaaaattagccgcgagttgtggcaggcgctg
taatcccagctactcggaaggctgaagtgggagaatcacttgaacctgggaagcagaggtcgtagtggccg
agatcagaccgctgagctccagcctgggtgacagagcaagactccatctcgaaaaataaaagtaaaaataaaa
taatgtactaactggaccacagagattttccaattgattattgacaacaaaggaatctgaattatttaaat
aagggtgaataagtagcatattcatatatatatgtatatgtgtgtgtattttacatttttataaaagtgtaaaag
tatatatacttttttcttctcaggtagaacctctcctagattgtcactgaataaacatttagcaataa
ctatggcaatcaaatcacatattgattgggtgcagagaagaattgaacattcaactctgaagcagtggtatt
tcttccatctgcaaacactctgtcccccatccttcttctgtgtatcctggaatccaagtcataaataatgat
aggtatttctgtcaaggtatttctcagaggagtgatattgaactcccttctcctgtacactgactcact
aagcagctacccttgtgaattccaattagcaatacttcttctgtatgtctgttccaactttcagacaaaacct
gtgttcaggattcctatagccatttatagggtgagacaggaagcattcagatatccccagaggtacctgata
accagctgataccactgtctgtcttgggttggccagcttgaaatcttgacattgtgtgttctcctccaga
gaaggtgccttttggatgtgagataaagacattatgactagatagtgcatgggtgaggggtgttttctagttt

2/86

gtcccagctactcgggaggctgaggcaggagaatggcatgaacccaggaggcggagcttgacagtgagctga
gatcacaccactgcgctccagcctggggccacagagcaagactccatctcaaaaaaaaaaaaaatcttttata
ctatatctttaatgtaccttttctatgttttagatacacaaaataccactgtattacaattgcctactgtattc
agtacagtaacatgctatatgtgttacgtagcctaggaacaataggctatatgttccctagggtatagggtatg
ggatccctataccatctaggtttgtgttaagttttatttatgatgtttgcatgacgacagagtcacctaagga
ctcatttcttagaataatattgttagttaagcaatgcatgactctattgactcatgaattcttaccacagacc
tatggggcagtagctattgttaccctcattttataaatgataaaaactgaggtacagagacagtaaaataactg
accacggctcattcagctactcaagagtcaaggctgggattttaaaaccagatcacatggtttcagagtggtca
cacttacctactatactgtctcaagagcaaggatgttttggttccacttgacaaatgaagatagggacctctt
tcattataagcctatttttaggctaaaatagaagggaaggggacacagtgaaatccaggccttctggcatggct
cctcagccctttctgagctggcctgggacagccttctcactcactgatgccacttctcactgagcgacttt
cctcagcctcactgatgccacttctcactgagcgactttcctgggctccagaccagtaagcgactttgc
ctgacccaccttattttgtctactcctgtgcttttatgctttacccatctgcctggaaagctctct
aacctttgaaatgggttaaaggcataaatgtatgctgggagaaatcctcagctcagggccaggcagcgtgctca
cgctgtaatcccagcactttgggaggcggaggtgggtgagatcactgaggtcgggagttggagaccagcct
gaccaacatggagaaacccctgtctcactaaaaatacaaaattagctgggctgtatggcacatgcctgttaa
tcccacagctactcgggaggctgaggcaggagaattgcttgaacctgggaggcggaggttgacgtgagccaa
gattgagcctctgactccagcctgggagacagagctagactctgctcaaaaaaaaaaaaaaagaaagaa
aaaaaaaaagaaaaaaagaaatcctcagctgagttgtcactcctcttgaacttctcagaccttccaggc
tgagtcgctcgtcattttgtgcttctcagttcctggcttctaccttctcatagcttgtttcatgtaattgtt
aattcttacttgccttctcctccttcttaagctgagagctacttcaagcatgggtaggacctagcagcgtgt
atgggacatgggtggtaacccgtaaatgtttactgaaaaaaaaatgcctaaagcaattgttaacatcatcag
atagataattatgggcatcagagattctgtctcaagcttatataaagaacttattttggctctaatat
cctgataattttctcattactttcacttattgtggcttggtgatcaattgttgacattttataaacatttca
ctatttgacaatgatgatactaaaatacgaattaaagcaaccatttcaagatagtgatgatgataacatata
cgctggtaacatcttattttcagccgtatcatggaatcctctgtttccatctctgctaggtaggcaggtatg
caggtagaacttgtagaggatgatgtttttgtttccatcttagatatgacaggaacttggaatttttgaca
taaatgacgaacatccgggattcttaacaatctttaaataatggatcacttgagttcaggagttcaagaccagc
cacgttataatcccagcactttgggaggctgaggcaggaatggatcacttgagttcaggagttcaagaccagc
ctggccaacatggtgaaaccccatctcactacaaatacaaatatttagccgggctagtgaggcagcgcctgt
aatcccagctacttgggagcctgaggcaggggaattgcttgaacccaggaggccttgagattgacgtgagc
tgagactgcgccattgactccagcctgggcaacaagagtgaactccatctccggaaaaaaaaaaaaaaa
aaaaggaatgcctttgggaataatttatttataattttatgtataacatatagacaaaccattagtttgtctt
atattttactaaatataaaatttagtaaatataaatatttactaaatataaaaaactcttagattttactaaag
agttacaactaattggcctggcgtgggtggctcacacctgtaatcccagcactttaggaggcagaggtgggccc
gatcacgaggtcaggagatcaagaccatcctggctaaacagggtgaaactctgtctcactaaaaaa
atacaaaaaattagccgggctgggtggcagggccctgtagtccagctactcaggaggctgaggcaggagaa
tggcgtgaaactaagcagaggcttccctaaaagtgtatctcaggataaaaggcagaggaagggtccatgact
gggattgggttgaggagagccagagaagcaagctacagaaaagagaaaaaattaatatgcaagagagtaaa
caacacgaaggaaaagaacccagtggtggaacactacacgtgagaaagggtgtctgtaaggatgttctacaaa
gcaaatgcttggatattaattcattgcagcaggagatggtaagcctcatgataaagaaggagaaaaaatcaa
gtcaagggtctgaggtactgaccaggtatacttgactatgccagcaactgtttagggggagatttgagct
acacttgtagcaaaaggcaaaatctgtaattagttgtaactcttttttttttgagatgggtgtctcgtctgt
ccccaggctggagtgagtggtgtgatcttggctcactgcaagctccgcctcctgggttcaagtgttctc
cagcctcagcctcccaagtaattgggactacaggcatgcaccaccatgccagctaatttttgtacttttat
tacagaccatgttttgccatgttcaccaagctgggtctcaagctcctgacctcaagtgtccgtccgcctcgg
ccztcccaaagcgtgagattataggcctgaaccacccgcgcctggcctaaagagatctaatcttagcaaaag
tttccacaggaggtctctcctcacccccaccccatccttcccacaaagaattagaacaatgtccctactacc
cctgctgtatctctgactttttacttttaaatctcagcagaatattttactaaatgttttgatgtggttatat
aaaatcatccctgctgacaaggaaacactttttgaaaaaagttttcattatcaaacagtaagtaacagtgac
tgccgtgacctttaacccatttctgagtcctccctcacttggaacttgggtggaggggactggtaaccaataag
tcaaatgctttaataatttatgcaagtgttgaaagaaatttgaaagtgaatatttctatcatcttgaaatgga
gaaagaactgtgaaacagcaagccagacgcctaaaggaaaagatttacagattaaaaataagattgcaatc
tggtaaaaatatttgcaacacatgtaacagtcagaaagtgaacacttgggttaacawgagcttttawcag
ataaataaggaaagaataaacattggatttttaaacaccgataaacatgaaaagatgttttaattctttat
atthaatccatattttttcagtttaatacaagaaaaataaatacaaaacaataatacattttatatatat
atatatatatatatatatatatatagtaggcataagttaaagactgataagactgttgaaaagg

gatgaaaaactaggcttactcataccaatatatatctattaggatggctaaagtaaaaaactgaaaatat
caagtgtcctaaaaaggatatggagcaattggaaccctcagacatcgctgrtzgagaaaaacaaatgggtacagc
caccctggagaacagtttagctgtttcttgttaaagttaaaccatgcgcttaccatagactcagcaatctcac
tcctgggtatttatgtctaggaaaaaggaaaaatttatacttgcacacaaaaaacttgtaagtgaatctttatag
cagctctattcataactgccaaaaactgagagaaaaatgtcctttaaagtgtgaatggataaaaccaactgtgc
aacatccatgtaaatgaaatactacttagcaataataataataatataaaaaacccagaaaccattgatgcat
gcaacaaatattggataaatctcaaaagcattatgctgagtaaaagaagtcagctgaaggatttcatactct
aggattccatttatataacattattgaaacgacaaaaattatggggacagagaatagatcagcgggtggcagg
gggttaggtgtgtggagaggggtgtggctataaagaacatgcaagggaatttttttgggagatgaaatggatc
tgtatcctaattatggctcatgggtaacacaaaatctatacatgtgttttagattcatagaactgtataccaaaag
aaaaaaagtcatttttactctcttaaaatgaaaaaagaaaaagcctgggcattctaacacctgtttgtgtgag
agtacacattgataccaagttttatgggtgggcaattttgtctataatacggaaagtttgtctgttctattat
tcagcaatcccagttttgcaaaactatgctaaagaatctttggggggccgggcacgggtgggttcacgcctgtaa
tctcagcactttgggagggccgaggtggacgatcacctgaggtcaggagtttgagaccagcctggccaactt
gggcaacccctgtctctactgaaaaatacaaaaatttagccgggcatgggtggcgcatgcctgtagtcgagctac
tcgggagggctgagggcaggagaatcacttgaacctgggagggcagaggttgtagtgaaactgagatcgtgccacc
gcactccagcctgggcaacagagtgagaatccgtctcaaaaaaatacaaaaaaatacaaaaaaatacaaaaa
aaaaactttgtgtacgtgtgcaaaagagaatacaaaagatgatcatggctgcatttttaaatgactataaaaa
agaggtacaaccagccaggtaaaagtgggtgtgcacctgtagtcacagctactcgggaggggtgaggtgagagga
acacttgagtcaggagtttcaggccagcctgggcaaccatagtgagaccctgtcccaaaaaacaaaaacaaaa
caccaaaaatgtctatctgttaggaatttggttttcaagttgtgatacataggtacagtgaaatattatacatctc
atttaaaatgatgataaaatctgtatttggtttacatgaaaaactgtccactataatgtagtgaataaataag
attacaacaatatatatggaataaaacttggtttagaacaacttctagaagaaggtacaatggacagaattta
tctctgggaagtgggtttataatgattctcattttcttcttcttcttcttcttcttcttcttcttcttcttct
tatgtctggacatttgattatgagcatgtattactgatctattttaaaaattgattttaatttttacaaaaa
ctcatgtaaaagcttgaagggttcgcatttttagaccatgttaaaattttccctggatcaaaacagacttattcaa
atatcttgtaccctgtcctccaaaattgcctgcccataacactacaaaagagagcatttagctgcatttt
tttggactgtgagatcaacaatattttaccatggccttaaaattttaccctccagtatgtgtgggttaca
acactcttccacatttttgaggcatttgccttttgatatatttttaaatgtaaattcagctgtgcgggtggctaa
cgctataatcccagcactttgggacgctgaggaaggatcacttgaggtcaggagtttgagaccagtttag
ctaactgtgtgaaaccccgctctcttttaaaactacaaaaatttaaccgggcatgggtggcaggcactgtaatc
ccagctactcaggagggctgagggcaggagaatcacttgaacttgggagacagaggttgagtgagccgagatc
atgccactgcccctccagcctggccacagagcgacactccatctcaaaaaaatacaaaaaaatacaaaaaaag
gcccaggcgagtggtcagcctgtaatcccagcactttkkgagcgccaaggtggsggatcaactgaggtt
gggagttcacgaccagcctgaccaacatgcagaaacccygtctctactaaaaatacaaaattagccgggtgt
gggtgtacatgctgtaatcccagctactcgggagggctgaggcaggagaattgcttgaacccaggaggtgaa
gggtgtgttgagctgagatcccgcattgcactccagcctgggcaacgagcaaaactctgtctcaaaaaaac
cgaaaaaattcccccaaaaaacaaaaaatacaaaaaaatacaaaaaaatacaaaaaaatacaaaaaaataca
ataaagcataattatatgcataatgggtgattgggaggatgaaatggaaagggtattttattactgacttcagaa
attatgtcctgatagattgatgggtgattttaatatataacttcttgtcaagcatctgttttagaatcaaat
actatgactctgcagtttccctgaaatctcatagtatcacatctctgttttgcttttgcatgggttttaagaaa
atgaggagtgtaaaacttcaaaacttgccttttcatgtattacatttttgaaatgacacactgggtcatttctta
gaaatataagggtgacaaaattttcacagaaacataagggtgctattatctcattcaatcttaggtcactcaaa
actctttctctccacacattgaagattcatttgggaatgcttttgtctatttgtgcacccccagtgaaagg
gtggtaagtgttttctattttgcttctttgtttatctacaggggtccattcaataaacaaggaggtggg
tcaaaactcaggctcttatgggtttggatgtaacttttgggtctcatttttagttaccaacagagaggtgtgc
ttctgacctcttgactcttccctgctgaatttactatgcttcttgatacttgtgaagggtgagattttcgag
gagtaactgtgtttttgttagaggttgtaattgtcttcttcttcttcttcttcttcttcttcttcttcttct
tcataagcatgtgcctaaaaaaatcagatgcaaaactagcaaaagttagaaactcagggtgacagctctttaaga
aaagatgcaattcttggggctgggtgaggtggtcttagctataatcccagcatgttgggagggccaagggtg
gcagatcgccccgaggtcaggagttcgagaccagcctggccaatgtggtgaaacccctgtctctactaaaaata
caaaaaattagctgggctgtgtgtgggtgctgtaatcccagctactcaggaggtgagggcaggagaattgc
tggaacctgggaggtggaggttgagtgagcctagattgcgccattgcactccagcctgggcaacaagagcg
aaactctgtctcaaaaaaatacaaaaaaatacaaaaaaatacaaaaaaatacaaaaaaatacaaaaaaataca
ttacatagttatgtaaaaggactatcagctaggtttagccttaccagatttaggtaattcatttctctgcta
cactcatattctcagccacttccctcatcacatttccagggtgcagtatataatagcgtcaactcgtgtaat
tccccctactccccatgaacttctaggccaaggggccacacgggtggggcatatagatataaaggagtaagg

5/86

taatagaaaacagtatctggaacattaaacgtaggatttttttttttctaatgacttactctcttattaat
atgtcagagaaaaagaatagctcctggctaagaaatacaacagtcctcctcatccagaaatcacagccaggaat
atggattcttaagtgtcaaaaaagtactctgaataaggaaagaaacgcagatgcactacttctattataata
agcgcttgatttcttttaatccctgagtcctaatttcttggcaaatttaagggtactgactgctctg
tgaatctattgttacacttgataatggatctgagttggggtaatatattgcctatcaatttgagatacttaaa
aatctctctctcttcttcatataccctctatctcacactttccatttaatgagggaaagtgaatttctttt
ttctgcccctcttctactgcttctagaataaaagcataaacaggacgcagaggagtgagatgagaggaagc
atttccaagcaatgggaaagtatgatgagagtcgtgagttggtagaatgggggtgagtaaggggtgggggtg
ggatggatggaagaggatggaggaggaagcaggtcatatgatcaggcttcaaaggcctccaatatcttgtt
ttcagaggcctttgtaggctcttctacagaactttgagggatttttcttgtgagcaaaggagaacatag
taaattttgagggatgggctgggctgggctcacgcctgtaatcccagcactgtggcaggcagaggcagg
tggtcatttgaggtcaggagttcgagaccagcctggccaaaatggtagaaacccgctctctactgaaaaaac
aaaaagttagttggatgtggttgcatgtgcctataactccagctactcgggcagctgaggcagcagacttg
tggaacccgggaggcagatgttgcaatgagttgagattgtgcccactgcactccagctctgggagacagagtga
gactccatctcaaaaaaaagaaattttttttttggaggggagaaaatatatgattagattgttttgtgtt
ggtttgccttgtttgttttttccccagcaaaaaatcactttactgcaatagggaagacaaaataggaagggg
aagaaactagagacaggaacagcagtttgagggttctgcaatacagaagcccagatgtttggcttgactta
gacactgggaatgaaaaataaatgatgaattaaaaaaataaaatatttgggaggtatacttgacctgacctt
gggtgcttttcaaatgagaagagaaaagatagagacagatgaaaaagttaaagcaaggatgactatgatttccc
atagtgaatgtctggatgatgatcattaaatgaaaatttttaaaaaggcagatggtagaaggagatttga
aggaaagacaagaaatttgtttgttttggatttacttgtagaatgacctgcaaaattttgtcctaataaat
ttaacaagtggctttccatacaaaaaacaaacccaacaaaacccctgatgtaaaccaaaaaataaaattctgag
gcccccttcacatctgaatgaacttctcctctcgaaggcactcttaaaatttaacatgaaagactgggt
tcaggtcatgacgggaagtgggggtcgagcagggcctcattatgcctctctggcattaaacatcaacacagacc
ttaagtctgttaagaagcatttacaatctattctctctgaagcctgctacctgaaggcttctctgcacact
gagaactttggctctccacaatcctttatcttaagccagacatttctcttctattgatcccaggctcttagat
aaactcaaccaattgtcaaccagaaaaattttaaatctatctataacctaagaagccccacttcaagttgccc
ctgcctttttgaactgaaccaatgtatttcttaaaacttatttgattgaagtctcatatctccctaaaaacca
agctgcaccccaaccaccttgggtgcatgttcttaggatctcctgagggctgtctcctgagggccaagatca
ctcatatttggctcaccataaaatctctaaatattttacagagttttactcttttcatcgacactgatttata
ttggattttccaatgggtgtaatatctatgccgttggcggatttcaagctagctggtagagatagcaaacaaa
caaacaaaacaaaagagatatgcaaaaacaaactcttctgagcttgtgtgctggctccaacacacacatgctgc
tggtatttctaccaggcagcataggcgccaggtgggtgagcctggcaaggagacaagagctggagggtacag
ggcttaaatgaagccaaggcggtgaataatattgatgaggagagcaagtagaaatgaaaagagaaaaccagt
attaggagatctataaagaaacaatagtcaaaaaagagtggttaagaggcagaagaatcagaagagaacc
agattcatgaaataaaagagaggaatcagttcaggaaggaaagtgtggtcagtagtgtcaaataccasaga
ctgaatagycctaaggattttaaagaggtcaacagcwcaccaatgaagcgggttttctgagcttaagatatt
tttctttatttttctatgttaaaaaatattttataaagaaaaagaaaaaagagatcacatttgccccccaa
ccgctccctggcctctctctctcttaaggaagtcgttaatgaatttgggcagaatagattcagagctgtgaga
gtgaaaatttgactgcagtgagggtgttaataaaaggagggggttagagatgaaatctttccagcagtt
tggtctctaaagggttagcttgaaggaaagaggggttggaagggtggtttttaaagaattatcactcacta
atcaactagaaatccagtggaatatgcagtaactgtctgtaatccagcagggttaactttttttttttttt
tttgagacggagtctcgctctgtcaccaggtggagtgagtgagtgagtgagtgagtgagtgagtgagtgag
gctcccagttcaagcaattctcttgctcagcctcccaagtagctggaactacaggcatgcaccacatgc
atggctaaatttttttgaatttttagtagagatgagtttaccatgttgggtcaggctgggtctcaaatctct
gacctcaagtgtaccccgctcaacctcccaaggtgctgggattacaggccagagccacagtgcccagcca
aggctaacctcttgatcccaatgacaaacagaacaaacatcttactcaagtcagaagcaataataatttg
aatcttgcttgcatgtcaacaggagccacattaatacagaagaggatcacattgggtccaattaaattgaatt
gattgagagcctctgcaatacacggctctactgcacaaataatgatggttctggtacatttttatttgacca
ttgattgtctgatttgtttctgtgtcactgtgtattggaattaaagctgactcaatttgaactgcaggtcc
ttttatccctctatt
aagatttcagctattaggcatttgtcttt
ttgcccaggctggaatgcagtgtcacaatctcggtcatcacacacccacccctccctgattcaagtgattct
cctgcctcagactcccgagtagctgtgactataggtgcaaacacczacgcccagctaatttttgtatttt
agtagagacaggttttctactatgttggccaagctgggtgcaaacaccacacacacacacacacacacac
ggcctcccaagtgctgggattataggcatgagccacgggtgcccaccaggtcttcttaatacaacaatt
catcttaaaacatcattttaaaatatatt

agagtttctagcaaccagtatcattgggtatttttaacaatgtgtacatgtacatttatgcagatgagttaac
atatatcaaagcaacctccaaacaatgccatttaggtaatctccaatttaaaagcctcaatagaatgataag
attgagcttttctgtagttccatgacctccagcagagctctgcaaggccacagctgcctgaaggttgattctg
taattagaagatgccagggtcatctcagaatagaacctcaagccaccaggtacatttacagaatcagcct
ctccagaaaaacagcaacaaaggagggccttctctatgtattttggaaggagtcacctagaggaggacttggg
gttttgggtgttgggtgtggggggcagggtatgggatggggagggggaagcttattgaaatatactaaaagacaa
accaacctaaagggtggagggaagaaaattcacacttgaagcttctttttaaggggcatctcttaggctc
tagcttttgagattcagtatatatatttttgagtcttgcctgcctggagtgcagtggtgtgatctgggct
cactgcaagttctgcctctcaggttcacaccattctctgcctcagcctcccgagcagctgggactcagggc
gctgcccaccatgcccagctaatttttttgatttttagtagagacggggtttcacctgttagccaggatgg
tctcgatctctgatctcatgatccgcccgcctcgccctcccaaaatgctgggattacaggcggtgagccacc
gcgcccgggccagtaatttttgattttatgaagatattacatttgtaaagtatgagcttgggtgtcagcaaaact
atatccctgtgtcaaaactggccgaatcacttagccactttgggccaatcacttagctcttcaacagtaa
gaaatcaacaagaaaaataaacatttcaaacatttcaaatgtgttcatgtattcactgtggggatgaccaga
ttctcgaaaccacaggttgttcttagtgaaacaagtttgggttggggccatagacttgtgtatttagaatca
atggctgttctctctctgggactttgattttttcttgggctcatccctttttgtagtatcttcttctgt
cttattttgtataggacttaactgttccattcccttatttagagcaatctaagtattaccttcatccttt
ggaattatatgcttcaaaattccaaaagaatgattttgggctgggcacagtggtcacactataatcca
gcacttttagagggtgaggtggatcgctgaggtcaggagtttgasrccawcctggccaacgatagtgaaac
cccgctctactaaaaataaaaaatttagccgggcatgggtggcaggtgcctgtaatctcagctactcggg
aggtggaggttgcaatgagccagatcgccacttgcactccagcctgggcaacaaaagggtgaaactccatc
tcaattaaaaaaaaataatgattttgggtgcagcttcaaataggtaggagaagaaggagagaggagatgg
agggtcasggagatctaattactctctaaaaatcagcttaggaaagataaacacttttaataaacactctctgc
ttttataacatcatttctgccaaggagctcaaagggtttcaacamagttcactttcagaaaacccctttgagga
agacagaatatacatcttctctcmttttaagatgaagaaacaggccgggcaaatggctaattgcctgtaa
tcccagcactttkaggaggtgagggccasargatcgcttgagctccaragtttgagaccagcctggataacat
ggcaaaaacccctgtctctacaaaaaaaatacgaataattagatgggtgtgggtggcatgcactgtgggtcccagc
tacttgggaggctcaagggtgggaggtcgcttgagccagggagtcaggtctacactgagccatgattggatc
actgcactccagcctgggttagacagagcaagaccctgtctcaacaaaaatgaatgaaagagaaagaaagaaa
gagtgagaggagaggagatgagggggaggggagggtagcagggagggggggaggaaggaaggaaggaaggaag
gaaaaaaagatgaaaaaagaaatagcaacatgaaacagaggcagaaagactttacgtaaattgtctcat
gtggttgtcaagtttgaccccaaaacccaatttattgaccaaggttattctttgactgagggcaggggggtcc
gctctcctgggcttgggcttttagaaagctcatctctggcctttctgagatccatccctttcttttatttt
tcttgacacggagcttctgtctgtcactcaggtcgagtgagtgagtgatctcgactcactgtaacctct
gcctcccggttcaagcgattctcctgcctcagcctcctgagataacaggcgctcgccaccacatctggcta
atttttgtatttttagtaaaagactgggtttcatcatgttggccaggttgggttccgaacccctgagggg
gagctgcccacttggcctcccaaagtgtgggtattacaggcatgagccactgcgcccagctcagatccatc
cctttctaaagggcaaacagttccatgggtgcaaaaggggcatgccaccagagttatgagtacctgggactcca
gaattccttgccctgggtggcctccacatgcacttccagggcctgcttgggctctctatgggtctgtcctga
gtgttgatagaaccactgatgtgagtacctgggcttgagccgtggcctggagatcctgttgactgtagcatg
gagggggcttgtgcagctgaatgtctgyatgcaggtgggtgggagttctggaatatgatggagctggaggtgg
gaagagaagtaggcttggggcagctctctcatgccacctcattctggccaaaactcaggtcaaaactgtgaag
agtctaaatgtgaatctgcccttcaaggtggctcaaaaggtatctttgtcaaggtaggagaccttgggct
ccagctgcacttccagggcctgcttgggctctcttacgggtctgtcctgagcttctatgzaatctgtcct
tcaggggcagattcatatttagactcttcacagtttgacctgagttttggccagaataaggtgacatttagtt
tgttggcttgatgacttaaatatttagacatattgggtgtgtaggcctgcattcctactctgcctttt
tttggccctccagtgatttgggtagttttgtctccctacagccaaaggcaaacagakaagttggaggtctg
gagtggtacataattttacacgactgcaattctctggctgcacttcacaaatgtatacaaaactaaatacaa
gtcctgtgtttttatcacaggaggtgatcaatataatgaaattaaaaggggctgggtccatattgttctg
tgtttttgtttgtttgtttctttzztzztzztztgtttttgtggcctccttctcaatttatgaagag
aagcagtaagatgttctctctcgggtcctctgagggacctggggagctcaggctgggaatctccaaggcagta
gggtcgctatcaaaaatcaaagtcagggttgggtgggggaaaaacaaaagcagccattaccagaggactgt
ccgccttccctcccccagcctaggcctttgaaaggaaaacaaaagacaaagacaaaatgattggcgtcctga
gggagattcagcctagagctctctctcccccaatccctccctccggtgaggaaactaacaaggaaaaaaa
aattgcggaagcaggatttagaggaagcaaatccactgggtgcccctgggtgcccgggaacgtggactagag
agtctgcggcgagccccagccagcgttcccgcgctcttagggcgggggccggggcgggggaagggg
acgcagaccgagaccctaagacacctgctgtaccctccazzzczzccccacccccacccctcccccaac

tccctagatgtgtcgtgggcggtgaacgtcgcccggttaaggggccccgggctccacgtgctttctgc
tgagtgactgaactacataaacagaggccgggaacggggcgggaggaggagAGAGCACAGGCTTTGACCGAT
AGTAACCTCTCGGCTCGGTGCAGCCGAATCTATAAAGGAAGTACTAGTCCCGGCAAAAACCCCGTAATTGCGAG
CGAGAGTGAGTGGGGCCGGGACCCGCGAGAGCCGAGCCGACCCTTCTCTCCCGGGCTGCGGCAGGGGAGGGCG
GGGAGCTCCGCGCACCAACAGAGCCGGTTCTCAGGGCGCTTTGCTCCTTGTTTTTCCCGGGTTCTGTTTTT
TCCCCTTCTCCGGAAGGCTTGTCAAGGGGTAGGAGAAAGAGACGCAMACACAAAAGTGGAAAACAGgtaaga
ggctctccagtgacttacttgggcttatgttttgttttcgaggccaaggaggcttcgggaagtgtcggtt
tcggggactttgatccggagccccacatccccaccacttgcaactcagatgggaccggaggcggtgttaaat
ggggagacgatgtcctagtacgagctctggtgacccaggactctgcgtgctgcgcttgzgggcttgcccg
acggtggagaccggggagcatctctggcggtgggagaccggcgagtaacccgggctcagaggggtcgggg
gttccccggzcggtgctgagggcgctgctgcggggtggggagagctgcaggtccggcaccgagzcgctgttt
gttcggaggggccctgagctggcztagzaaaccttctggttgagggtcggccagtacctacggagacaaatg
ccagcactgagttcttcaactcggttcttaagaagctggtctgttctgacctgggaattggctatatgtcccc
gggactggagcgccacagttccggactgtgaatccgggaactcgagttggaggtgtcccaaacgggtccgtgg
tgctattgtctactagaggccttgggtctttgtztttgacctgaggggttagggagggtcctgcctacagtctcc
gtgcgctcagctgagctggtgtccctggcgagagcgcgagcagagttttgttttcttttttttttttttt
ttctttcttttaagtctcggtctgtcgccaggctggagtgcaatggaacgzatctccgctcactgcaacct
ccgctcccggttcaagcgtattctctgcctcagcctcctgagtagctgggattacaggcgctcaccaca
tccagctaattttttagtatttttagtagagacgggggtttcaacttgttggccaggctgggtctcgaacctcga
cctcaggtgatccacggzgcctcggcctccccaaagtgtgggattataggcgtgagccaccgcgcgccg
agttttgtttcttttaaaaacaagacttaggagagctcgaggagacccggaggtgggggtgcccactcctcc
tctcccaggttccctgacccccatctccagaccgttgcgtggtctctcggggcagcttctgcctgggc
gcagatgggggaagctggggcgaggtggtgcccgtggaatgaccgggagtaaccccgcgggcgcgagaaact
cggagctccgcccgggggtcgggctggggtctgcccgtgaggggtgggggtgctgggcgcgcggggtcgggtgg
zccccggagactggcccgagzgcctcctggccggaggacctaaggaatcggccggctctactaggtgtctt
tgctcgcggttccgactgtgaatccgggtgaagacgggtggttgagacggggaggaactataggttgaggg
gaaagccggtttgttt
gccattgggtaaagcaggaaggttcttggggcgcgagcgggtgcccagggttatgtgtaggtgcctcttaggt
atatcttttatcaaaaagaagcaaaagaaatagattaaaaataaaacaaagaaaaaagtgtgtggcactggc
agtaattggcctgcctttgcagcactgataccattagcttttaaaatccgacttttctattgacactcaaga
agagaatgggtagatatatacacattcatctcatagtggaacaaatttcatatttaaaaaaaccttctgggtac
tgaaatcagcaagtcaacttgcctccatggccgaatccctgcttcccacgaagagaacctcacaaaaatttc
ccccaggttaaagagtgggaattttcttgatttttttztcttttttttttaacggccgtagttagaazccc
agacttaaattatgatcttcttttcaaaacaaacttaaaagtccttaagttttcatctccccttttattcaa
cctattcttctcatacctaccacaaaaataatggaggctttctgttgagaaactttccgtttctgttgagag
tatcattctcttgagaaacttttctcctaaatcagagaaagtatggaagcatggaaagtattcctgagtagaa
cctctacagatattacaatttttcaaatataaagtttccattgtcagcctgtttcccaagtgcctccaca
aaccattaaataattccacaaaccattaaaataatgctaggggaatttttaggaaaacattggtttacaa
tcagaaggaccggggaagtgggtcttcagccttcacgatgactacaagccatttaagggaactagaattgcta
ctgttgtagagcaatttaggagctctgtatttgagcaccgcagataggttccagaatgacatatctgactgt
aacctggacacgtgtgatatgtgtctcccctgcagatgagcatttgaaatctcaacctcgtatttctacg
agtgcaggcctataatggaccctgggcacatt
ctggagtgagtggtggcagatatgggtcactgcaacctccacctcctgggttcaagagattctcctgcctcag
cctcctgagtagctgggactataggcgacgccaccatgcctgggtagtttttgcattttcagtagagacag
agtttaccatgttggccaggatggtctcgatttctgacctcttgatccacccgcctcggcctcccaaggt
gctgggattacaggcgtgaggcacccgcgccgacccctggacacattttgacttagaacatattttcggttt
gtgtgagacagtgcattagtgaggattggaaaagagtgtcaggaattgattgttttcaaggattggttcc
ttctgtctcaaggaggtccattgttaaacataaaaaaatgaatgaaactgaagaagttcagtgacttagcttt
ttattatctctgtagtagtacttactttttggagaggaggtggttgggatattttccatttaaatttttttt
ttaaagggtatcttctcctcctgaagccgggatacttaagctatatatgtagtggttcaaaattaagggtcttc
actgttttcttttttagctgctagaataagtgaacattaccttagatagactcttctaattatgaagatatc
tagatgtctagaaaatatcaaaatgcatgtgggtttttgcatttctaaaataacttttaaaaccaaatactttt
tctttttttttttttctgagatggagtcttgcctcttttgcttaggctggagcgagtagaatgatcttggc
tcaactgcaacttcgcctctcaggttcaggtgattctcctgcctcaacctcctgagtagctgggattacagg
tcgctgcccaccacacccggctagtttttgtgttttttagtagggacaggggttccacctgttggccagggtgg
tctcaagctcctgacctcaagtgatctgcagcctcagcctcccaagtgctgggattacaggcatgagcca
ccacacctggcctcaaatacatttttttaagtatccagatatataaataaataaccattatagtagttgtt

atgggtcatttactctagcatcaaagtgttaaaagatcattctgaacacttggtttgtttatgctgagagaagg
cctactccaaaaaatgcaaccatcttcgtatctgcatgtggatacaaccatgaatggccaaagtatttgcaag
tggtgaatagacacttatatagcactgtgtggcaagtactggttgaaatgttttccagtggtttatttcattg
tatttatttttgagatagggtcttgctgtgtgacacacatcagcctcttaaggagctggggccacagggcacgcacc
acctcagcctcctgcgctcacgtgatcctcatacatcagcctcttaaggagctggggccacagggcacgcacc
actgctcctggctaaatttttacaattttttgtaaagacaaggctctcactatcttgctcagactgggtcttga
actcctgggctcaagtgatcctccacatcagcctccaaagtgtggtgattacaggcataagccactgtgc
agggtcatcaaagtctaattgaattttcacacaaaaccatttattgtccctagtttacaagattaaagtaaat
gagaagctaatttttctggctatataccttgcaaggccagagctaagacttgaaaccagcagagtctt
ttaactccagcactaacatttccagctgctgcaaccagggagcttttcaaggatgatcaccacatttcttaca
ttcatctgctataatccttatcagaatctacagcctgtatcatattttccttggtgctgtgagtggtcagc
caaattctcttttaacttgaaaccttggttgctgtagggattgcaacatcctggaaagaatagaataaaattta
ctcaactcaatttttacttggttcataatgaaaactataactattgcttcagtcagatggttgcgaaatagct
gtgtgatctcaaaatgttttctatgtgatctatagzaaaatggaatgatagagtattaggctgtaagggcc
taagazaacaaaggaaaaagagaagtgaactgttagtttagttgtaaaacctaaactttggtgaattgtaaaaa
atttggtataatacaaatatgattcttgcttgctcctgtccttgatgaagttgtggacctttgaaataagcta
tttctctgttactgctgttactgtttagaaatcaaatttagtttttcttaagataacgtatttttggag
ataaacacagtttcaaagtctgccttggttggttggtgcaactggctcattgtgttatccacagactttggg
aggccaaagcaggaggtacacttgagggtcaggzagtztcaagaczcagzcctggcaaatatggtgaaaccc
cgtctctactaacaatacaaaaaattagctgggctggtggtggtggtgcttgtaatccagctactgggattgg
gaggtggaagtagaagaattgcttgaaacctgggagggcggaggttgcaactgagtcgagatcgtgccactttac
tccaaacctgggagcagagtgagactcctgttgaaaaaaatgtctgccttgtaaaagtgaataggatga
gaaagtgcctttcttattaattggtgtaattgaattagaaataaactctttgaagacacctcttggtaaaaat
agttacattttactggtgatttatgggtatgttggtatgtttttaagttttccgtgtaataactcagttcatt
ctcatgagtgaaataggtgcttttattgtctttatagatgggaaactgaggtataggcaggctaggtacatt
attatggagttcgtgaagtagtgagctgaagtcgcatccagacagtttggtctccgtgagtttaccactct
catgttctcatttgagtatcttccctgaaaatagttgcctgaataagtagcctgcatagaaaggtacatttt
agaaatacttgaggccagagaatgaaaagcttacataaaaattgatttccgggtggggccttcagttactctcc
attctacgaagaccacaaaatagcatccaggcaagagcatttatccacaatggaggagcactggatttgg
ttcctaaaaacaaaataaagtgtgaaatcctgtcttcccatggttgaaaacaaagtgggtacaaaacctttta
gcttttgcaaacctcctttaaagaccgattttaaattgcytccctcctcatgaagctcttctggatccactcyt
tccccactcaagttgaaagtaagatcccccttctcttacttccattagacttggattacagcactctttgt
atcatgtatttaattctgttttttaattacagtttaacatttatttgtcttccctcttgagtgatgcttctct
agaggaaaggtctttgattcattctccccctggccttaattcatcccacttaatatggaaaaaatttaaat
gctgacttgaataagtccaacaaggagaatgggaagctcatggttgcttccgtcttctctaaagactactta
agataacaggggtaatcacagaaaagcattagaaatagagttatatgagaaacaaactgtagtttaaggctaggt
ttatgttagactgagaaatttttagtgcatacttaagttatttagggccaggttactttttgtagaacaaacat
ttcagtttctgctcagtttcttccgtttctgzaggcagctgtgatttaagaaaatgctctagctctgtggca
ttccatattcaagtactttgagttgtatattaattttattttgttaataagagtgacatgactcactaaagta
atttagagatttaaacacttttttaaaaaaacagtaacttcatatgcattggatctattctctataaagctct
tttcttggggggtgtttgtttaaaaattccccgggtgtttctctgccaatccaacttccaagaagcatttgg
aagtcaaaacattttatctggttagtcttaagctccagatattttgtgtagctggtatttagtttatgata
tttcccaggaagaaacttttttagtagttgaaccatttatgaaagacttccctgaaagctaccttagagagttga
tttagttcttccctaaatagtaaatagaaatattagatttaggacatcttgagtagatgcaaatattggt
gaaaaagaacatggatatacagagtcaaaatattagtagatttgaattctggttattactaatggatattctgac
attaggcaagttgctgatcactctttgcctcagtttcatcatctgtaaaataggattttgtgtttgtgtata
atgtgaaccgtataataatgcttggcctatagtgaattttatccatagagtggtttcagtgattttaaa
agcttgctttaggccgggagcagtggtctctgcctataattccagcactttgggagggccaaagtgggcgat
catgaggtcaggagttcgagaccagcctgaccagatggtgaaaccccgctctactaaaaatacaaaaatt
agctgggctggtggtgcaagcctgtaatcccagctactcaggaggcttaggcagaagaatcgcttgaaccc
aggaggcagagattgcaagtgcagccgagatgggtgccaactgcacagagcgagactccatctcaaaaaacaaaa
caaaacaaaaacaaaaatcttgctttatagtttacttccacatcaaattgtctttatcccatggttacttgc
tgatattccagacatgaaaagaaaaaagatgataacaaatgacagttattaaattaggttccactcttattc
tagatcaccaattctatattactattcagacttggaaacattaaatttttagttaaacttttttcaaatatgca
tataattgtcagtggttactatattttggggaagagattgttgacttctttgaagaaagatacggattttct
cttcagaaraaatacacatgggctcatataatccaaattttatgtgtaattacagggtgttcatgaatgcc

acaaatccattaagccatgtgaccttggacaagtcattttacttttctgttttttaggttggttggtctgtaa
aatgatactacttgacttttaagagcccttcaagctcttatgtcctctaaccagggtctgtattcagaag
aaggggttggtcctttaattagagccatctagagatctgaggaacatgctgggcattagtgtaacataccatg
tggattttgagaggtaaagaaaaataaccagggaatgcctcagagcattcctgatcagatcgatgacagaa
gaaaggaatgagaggagaggaagctgttgaaatttctctatttacctgctttgagtgaatgaagatttg
aatcatagaaccagaaggggttctcatctgaaatgcaaaggaaggaggagttggtttaattcaataagtttc
agttgagtaaacatgattttagtgagatactgttcttgcttctgactcaccatttggaaaatctctctaaaat
aaaattggactctccatctcggacatcatttgggtgtagggttttgcttttttttgagatggagctcgt
tatgttgccaggctggagtgagtgaggcgcaatctcggctcactgcaacttccgctcccagattcaagcag
ttctcctgcctcaacctcctgagtagctgggactacaggcggtatgccaczcactgtccggctaatttttgtat
tttttaatatagagacgggggtttactatgggtggctaggctgggtctttaactcctgaccttgatctgccc
ccttggtctcccagagtgtctgggattacagatgtgagccacagtgcccgctaagttttacttcttataat
ggactcctgttaagccaataggtgatgaaaggaaccaataaccaactctcaggctcattcctcacaaga
atagcatgcttagtaaccatcctaggaggagaattggactatacctcatgaggatagttgaagtatctcaga
agacccctcactgggggtaggctggtaagacacaaagctttctaaagcactgtaccaaatttggtgtttgaga
gatcataacaaattagaagtggaaagaagaggagtaaaaggaagaagaggtttctggccaggagcaggggag
ggggaaggagctgctaggaagatgtttgggtgtcatatccctgttcaccttgctttgcaaaattctgtgag
gatgccagggtgggagtaattgtttttcacaaagtgcaaacacgcttggtttctgaagaagcaagctctt
ggaggggtgggtggcttgaaatctgttggatctgggtatttaggtgatcacctttgacataaaggzcaacactga
tgcaagcagcagctttccttggaaggcaggagaaagtgaaggcccagactgatgagcttacactgacctg
cagaccttctccattcccaggcatgtttgttgccagaggtttacctagtgggggttaggctgttctgtggt
actgtgagagagaaggaagaagaagatatgatataacaacaacaatacatatttatattgaaattaaat
gcactaatacacctatagtgtctattaaacaaatttatttggttcagcaaatgtttgttaaacacaaatgtact
gtggaaagtactagggtgtggacagaggtcaaaagactttttaagaatctgccaccattatgatctcttct
tgcttggcattcaaggctctttgaaataagactgtgacccactttgatagttttgtcctggattataagaca
catgctcgaaggaaactatagctgggtttctcaccagactgattaacatatagtatgggttggtacctgttaa
atgagttctctctacaggttttcatcttctacttttaagaaccccttctggcattgtttggctcctcattg
ttctggaatctcatgttccatctcatgtatttgccttgggttcacacttgatcttctgctcatattcctcacct
actgaaattttaccatcaaccagaccgtgggtgatggaacacagcatgggctagtcttctcttatatatgat
ctcatttaattttcactggaactctgagataggtagcatttcagcccactcaagttgactcaaatttttgta
atcatcaatatatttttaataactttatatttgacctgtaatttgaaacaaatagatttatcataaagt
aaaggttaatttttaaaataattaggtatgaagacaaattatttttctcacagttctatgtataagataaactat
tgggtcccaaggccctcagctgacaatgagacttctctactttgttgaaaagggaattagcaagcattaaa
gaggtgtcaaaaagaagactaaacaaaagcttactccttttttttttgagacgaggtcttgctctgttgccc
aggctggagtgagtgccaccacctcggctcactgcaacctcttctcctgggttcaagcgattctcctgccc
tcagcctccctagtagctgggattacaggtgcatgccaccacaccggctaatttttgatttttgacagag
atggggtctcgtcatgttggccaggctgggtctcacaactcctgacctcaggtgatccaccacctcggcctccc
aaagtgctagaatcacaggtgtgagccgcccgcaccggccgcttactcctaatgtactaagaatgttatat
ataggctgaagaagtgtgaaaagaaccatattttctcatgatgtgggttcaatgtttaatactgtgcttgtt
catctcctaaaaatcctctgaatatcacttaaatcatcctgtgtgaactctccacatttggggaaatactga
gcttgccctattattattagccccatatttcagatgatgcacctgagccgaggagaagttaaataacttgt
tcatgggtccatatttggctaattggcagagccagggttcaaaactcttgctctctgactcccagggtttgtg
cttttccacttggtgaatttctcatgtactcctccataaacaccttctcctagaacttttaagggaatgct
tcccctgttctctcatagcattttaattgtaagttgccaaagtgtcccagtttgccacctaccagcaatgtg
ggagaaaatagcaacatatttttgatgttgggtgtacggtttctctgctcttgggatgtatat
tccatggctactgaatacccaagtcaccaacagttttcttgactcagaaggtcatccacttcagcttcttc
atcaaaaagacatattttctggctgggcacgggtggctcacacctgtaatcacagcacttggggaggtggagg
caggagaattgcttgaacccaggagggtgaagttgcagtgagcccagatcgtgccactgccctccagcctgg
gtgacagagcgaaactctgtgtcaagaaacaaaaaaaggacttgtttctgttccattaccacagtggtga
taattggcgtgcttaaatatttctccagctgccatttaactgcaaattaaatcttagtctcttgctctttaa
tccaggcttctctatactataaccagaatttaggataactattacagtgcctttataggagagaagaagaa
attgtgtctgtagatgtctgttcttccagcttaaaatggacactgaaatgttaaatattggactggcctca
tttatttctcctgtctgttgggttcaatttgaatcttaaggcgtcttcaactggaattttttgttctctca
actaaaaatgttcttctgaagtgtgaatcagaacaaaatcctgaatgttgagggtttcctaaaggctgttt
ctttatgcaaaagcctgaaacccgatgttgatgttggctgttaaaatcaactgtgaatcaaggcagggttt
ttatttttatttttttttacttttaattgattgtgttaattatagtgaacaccttgagttcacgagaagaaa
gccttgggtcaagtattgtttattaagttgtcagctctgttgcaggatttgcaatttagtggaattagtgc

catttttcagtttacaattccagtcacatttcacatgatcagagcatggctttcttctctgtggagcaaata
gagggctgtctgacacttgggtccagtggtccatttaagcagagtggtatgtccctggagctcgcagaga
agggcatggcactctgaccccagatggcactccgttttgggacattgtccaatcttagttcatagcatatgt
gaccaacaccagctctcacctgatgtaaacacttagcgctgtgtgcttgggggattggattgtgtgaattt
ttcaaaactacagttgacagaaggaggtaccaaaaatgaaacccaataattccatttttgggaattattcc
cacttttgttccatttttccacttggttctttggcacacagaatgtttgatttgtgaaaatcttaataaca
gtagttttttctataaggaaactcagaatcttgataatattggaataatacagatccttttgttaggatcct
ctcagacctcatataatagagttcatgtagtcaatatttaagaaaaaacacccttaagtttttgttttccag
aatcacaagtaagtggtattaaacttgtgatcttattcccttttcttcttaatttagtgaggcagccagc
gagaggggtttgttttgggtatttctaaagaaggagttgtctgtaagtttggagggcaagacttagactctg
tgtctctgtgcttggcctggaaacttggattaaattgtcactaacaggagttagctggcctcgccgggctgca
gaaatgaagtgcttggcacacatgacatattgactgtctcaagagctggctgggtgaaaggacgttctggaga
aggctgcccagatactgtatgaactagaazctggacaagagcctggagattggataactcagtttggcgcaagt
aaaggaataaaaagtgttaagtggtgcaaaattgtatccaggtgtttataggctccctgagttcctgactga
gcctatctatgggttttagagttcaaggtctttaccaggtgctgacaatcttatactctaggttgaacctccg
gggaaggtgcccctgtcttgatggcatgtttaccaggggttcttagagcctcaatcacagattctctctagctc
acatgaagtttaagtgaatgaatgtgtgttccctacaaattagagagggtttgaggaaaaatcagattaaatg
cactcctgcttgaacttatgtttcttagaacacagctggaaatttgtcacacaaaacctttactttcagtga
catttcttgactgggtttgttactgtagtgaatctgtcttaactatcttttcttatcgctgaggtttacttc
cattctacatgtgattgtggagcgctgcgtcattgtgggttctcagtgtagtgaggagtaggaagatgggtgaga
cacagtagcttgttgacattgtcttaatttatcagggatcactgatgagtttagtacctagagaagattgta
ggtagagctgaaaaagatggaggaattataaggctcagatttctctcttttttttttttttaagatggaggt
tcactcttgtgtccaggctggaattcaatggcatgatctcggtcactgcaacctctgctcccggttcca
agttagacttgatgggtctcacttgatgggttctggctcagcctcctgagtagctgagattacaggcaccga
ctaccatgcccagctacttttttgtatttttagtggagatgggggttttatcatgttgaccaggctgggtctcg
aacttctgacctcaggtgatcacctgcctcagcctcccaaagtgcagggttaccaggcatgagccactgcgt
ctzggccaaggctcagatttctaataagagatzttctaattggacatagaggctggaggaatgggatzzggaca
zggazaaactgagtzczaggtgccaazzaactttagggggccgggtgcggtgggtcagzcgzccztgt
aatcccagcactttggggaggctgaggcgggtggatcacgaggtcaggagatcgagaccatcctggctaacac
agctactcgggagggtgagggcaggagaatggcgtgaagccgggaggcggagcttgagtgagccgagatcgc
gccactgcactccagcctggggcgacagagccagactccatctaataaaataaataagataaaataaaata
aaataaaaaacttgtaggggaggtggcagtggtctatggaggataggtgcaacctctgtgagaatgttagagaaa
atagataaagttagtggtgaggaccccccaagggggttttatagtaaaacaatgggtcagaagtggcaacag
gataccgtataatgctttcacctctaccaatgcactgggtactggagagcgctccagtttgcctctggaaagg
ccctttctgtggacaaaagaatacagaaaaagagattcctttaataaaacccaccactctgtgtcccaccttga
tgaatacttctactgtgaaattgcccagaattaatcatggtaatagctactgtacacttactttgttccaggaa
ctggataaatgttttacatacattatcagttctatttttggagaagatacaggggctcagagtccttaggg
ttccagagctgggtgagtagcagagtcaggattcaaacccagcttctctgactctaaaacctcctttcttcc
tgctgaaacaatttaactcaagacaacaaaggagtttaaggatttggggagtttctgcatggtagaatagacc
caaaggaaaagaaaagaaagacagtgactaagatttgggttgtctgccccaccaaatgctttgagcacttcc
ataaatataaatccttcagggtgggagaagggtgaacatctgaagacactgattcttcagagatgtaatcca
aacaagtgtatcttgggtgatagggtcactaaacctattatcccaaaattctctggaaaacggtcctataa
cagcaggggaacattatccagccaagttttctgcaataaaagggttgctgatagaggcttgctgtgtgt
ttctzgtzagcztzagggtgtttatgaattcactaatcccttcccttcagatcccttttattctgggtgta
tgattgtgactgzaaaaaaattgattttttttctatgacatagaatgttgaaagggttgatttctttctaga
ggaaagattcttttttctatgtgctacataccccccgaccagggaagggcaaatagtggtattgtttgct
gaagtccttcttgaagggtgttgggtgtttgcttagtggaatcagcaggggaagagaggctatctctzaa
cattttgttagazgtttcttctgagttctatagtgatgaaacaaggacttggggtaaggacagatctgct
ttcagaaatcctggctcttgtgaggtttagaagccttgagaccatttagctgggtggcaacgggaatgttgag
gggtgataaataggatcttgggtgttccaagtatagtgacatgatataagtgaggttaaacctttaggatct
ccttatttatttgggttatttttgagacagggtcttgactgtagcccagggttgaggtatgggtggcatg
ctcataactcactgcagcctcaaactcctgggtcagcgatcctgctgcctcagcctcccaagggtttagg
attacaggcatgagccgccacaccgggtcaggatctcctgtaaaattatattgttgacaacatgaagaatta
tgcttctcaaaagctagttatagatttgtacaatattcatagatttcttgtttcagtttttacaattcata
gcccttattttgaaaattagctattagcaataattttgtctaggaaattggatgtgtattcaagtgaagaa
ggaagtacagttacctattatcttattgtaactaacaatcaagtaagtggtgatgcatttgggtactttaaaaa

ctgcacccaagttacagattattggaattaataaaattcactggatctatatatttttaaacggacagtgtg
atagcagaacctcttatagaatzgatagaattcctctggaatgattggataacttcatttcactccttgactt
ttaccttggaggatttcttaccctcttggctctcctcaatttgactattaaaatggttgcctttaaaaatagg
aacacagtttcaggggggagtagcagcccatgaccttctgcaaggccccctaactcaaggtagtttccctg
gaactgtggtttatggaatgtttcaggagtgtagggaggtataaatttaaggctgtcctagcaaggataacct
taaggatagaggggccagtagcatctggaggccagaaaaggtazaactgaggcagtcagattagcttczag
ctcaattaagctgatgggtcagcctgggagaaattgacagtagactctcaatatccctcccacccacag
cagccacagctctgtctgtctttaaactcatgggtgcagtgaaacctgttcttccaggtgcttggcctcagta
accttctttaggtctgtcctgaacgtggctaccgatccaaagacacatgatcagagaggcaattagagaaca
gaccttttccaaagcaagcatgttctgttgggtctagaagtttcatgtcctaattattataggacctgtgca
tctctctggagatgaggcacatgagtcatactctgtgattcttgcctttgtgtcaacatctcatgaataggca
atcagagcttggcaccaatgtatttccagttcatactctgatgtagtttaaatccacctcctgtcttgtagtt
tactggcaagctgtttttgatataagacatctagaacactgtaaatatataacatttttatttgcctattat
acctcaattacgaaaaagacatctagaagcaacctcatcaagagagatactgaggccgggcatggtagctca
cacttgcaatcccattactttgggaggctgaggcaggttagatcacttgaaggccagagagctggaa
ggccaacatgttgaacacctgtctctattaaaaatacaaaaaagtttagctgggcttgggtgggacagctgt
aatcccagctactccggaggctgaggcagagagaatcacttgaacctgggaggcagaggttgacgtgagctga
gatcacaccactgcactccaacctgggacacagagtgagattacatctaaaaataaaaaataaagtaataaaa
aagagagatattgatagctgttgggtggaatttcaacttccatctcacttctggtaacttttggaggttg
ttgaacaaagtggaaatcacgcacatacacacacacatactctctgtttgttttaaggttaatagaata
gctgtcatataatcactgtttttgaaagaggagaattagttgtctatctgtacattttgggtatgtgaactat
ttggatagaactctgagaaatgcattcagaac
gcatataagagttgttgaaaaaaggtatttcttgagaaaccagctctaatgctaggcaagtcacttgccttgg
gggaggcctcagcttctctgtctataagattgcagcaggggtgtagtggaatgagcttcaacattccaag
agattttatctactaatcagacagtcacaaatggagcatgacttgggtgaagcctctcctcttccaccagagg
ggccaatttctctgtcccagtgagatgttgacacttgatagatccctgcttggagacttccctcttctggaa
cctgcccctggctcaggtcaggtgagggctgactgtcaccttgcagtaggagcccagcactaaagctcatgtgtg
gcagtggttcttgcgggaaggaaaaagaccagccagccatttgttactgcacaagcaaacagcttctggtag
ctgtacagatacatgcacttcttctcctcactgtgtttccatagacagatttagtgctgtagaagatagag
ggcagtcacgggaaggagttcctgttttcttcttggctatgccaaatggggaaaaatcctcctatctgtct
tttttagtgctcatcctctctcccttcttcttcttcttataattctcatctctcctcctcctggaaatgtgc
atgtcaagttcaaaagggcacaaatgttttgggtgaggaagaggtgggagaaacacgtgccaggtgctaaactagg
gtcatcatttcccccttcacagccagcttccctgtgaatgtgtgtgtgtgtgtgtgtgtgtgtgtgtgtgt
gtgtgtgtgtgtgtatttcttcttccagcatcactgaatctgtctgtctgtgtgtgtgtgtgtgtgtgtgt
ggaaaagttaaagtaatttataatcccagctgtctattttaaagccaccccttcttgggttagcatatggtcca
ctctctcagttcattgtctcctaaagatgcttcatcagaaaggaataacttccaccccggttactctctgtcccc
ttactctgctttatttttcttctgtcaatcctaccaccacccacccactgttgaacaacccactattatttgt
ctgtttcccatccctggtagaataggagccccatgaatgaaggaacttggcttctgttgttccaccactgaat
ctctaagggtatggaacacacctggcatgtgataggcactcgataaaatatttgttgggtcatgggcacctt
gcagagtttaaggctcaggtgttgggtggaattataagtggtgaatgaatatttactactattcctcttcca
aggcatcacacaataatcaggctttacactatccagttcttaggtcttccaagttatgacttgtgaggtat
gttaattatgataatagaaggcagtttatttgggtcagatttattgatgtgtaatttaccacagtaagactt
cccccttacaaggtatgatgagtttggacaaatggatcacatgtgtatctaccactgccatgctcctttt
cagtcgtctgtccccctccacccatgaccactgggtcaccactgcagtgatttctgtcccccttatttccacct
ttccagaatgtcatataaaatggaaatcatgcagtagtagtttttgggtctggctatttttcttagcatta
ggcttttgggattcatccaggtgtgcagatgtaacagtagcttattcctttttatggctgagtaaggtgtccc
agttttatttataatatttattttagggaggtgtctcactctgtcaccacaggctggagtgcggtagcgcgat
ctcagctcactgcaacctccgctcccaggttcaagcaattctcctgcctcctgagtagctgggattacagg
caccacccgcccagcccaactaatttttataatttttagtagagatggggttccaccatgttggccaggtga
tctcaaacctcttgacctcaggtgatccgcccacctctggctccaaagtgttaggattacaggcatgagcca
ctgtgcccagccccagttttatttatttaccaggtgatgggtcttttcgacaactaattgtttccagtttttg
gctattctgtataaggcttctataaaatattcacaataacctaggatgggatgactgggtcatataatagtac
tgataaaccttagcagaaactgtcaaacatttttccaaagtggctcttccattttacaattccacagtgat
tgagtcocagtgctccatacacatgctagcaatttataatttattttagtggtatgtaatgatattctca
ttgtgggttttaatttgcatttctctgcagtaaatgatgaggttctgtctatttgggaagggttttaattta
gcagtcgttgtattctgtagatattataaacttcaaaatcatcagtggcatttgcagttaaaatttcccttaa
aaaattggccaaaggtttccagcagtcacttctgccatgccccaaactgtatgaacaaggctgaggtgtgga

gattgtcacattttggcaaggagtgatccacttgggtgactgatgagacccagagagcgtacgcctcgggct
tgaggggtgaggacggggcggaagtgcactgcatggccctgctggccttgggagggctgccagtccttagcta
aagctggcagttatgggaaacagacttagattctattacgttttccaggatgtcccaggagtcacctgggaa
gctcagcagtcctttgtgactttcaagcatatggtagaagctgctgaacacagagctccctcttggggata
atttgcacaaatcatttaatcaggcttgagaaatgagttaccacagggtccaggagtgctgccacccttgaat
tctgacaccctatttctcctatccgtctcttaattaattaagcagacatccccaagtgcctacgacaagcca
ggacccttttgcataactaaggaaaaacagggatgaaggaaacagaaatgggtctctgctctgactcagaaggta
gaaatcctctttcccagccaagtcttccctaggggagcagtaggaagggtctgaacccacgtgctcagtgcga
ggggaggatcagggaaaggacattgaagaagtggagacctaagtttgagacctaggcatttagccaggctag
cagtgcttgaaaaagtgtcttaggacaagagaactcaccagtgaaagtcacagtggttaggagagcgtgcagca
tattctgagcctgtatcacacatctccagggcattgcttagcaggtggggagtgaggcaagagtaggctggag
tcacagaaggaggccaggtagacctgggtgagcctggactctatgttcagggtgctgaggagctggcaaaa
ggttttaagtcggggagaggcatgttcagatatgtgtctagctgagtaacttgggtgctctgtgacaaat
gggtgggagaccagtgagggtggcagttgcggtcatctaggagcaggatcagagtggtcctattgactgggatg
actgtgaagtgggatcctttccagccagttaactggaaatgtgtatgagggcagaagtgagtgactgactgtt
gaaacattgagaaatctagtacatagtactgtctcttttatatcttttttttttttttttttttttttttt
tggtttgttactaacttggaaaactgatgtggaaatgtccctttggcttcagttacctgagcagaaggggcc
gggcattggccaaactctcctcttaggacagaattgctcccagttatgatcattgtgttctgagttgggggag
caaattgtgcaggaggccagggtcagtgccaaagtggggtgggaggaattggagcaggaagcttgccaaagtgt
gcccagcaaaagccacggtagaactttctactgtggctctatgctacttcttagcaaccttctccatgtgctt
cctggagagtccttggagtcagaacctttttcttgaaacccagacacttacttccaagaaaatgctgtcca
agaaaactcatccttcccttcttctcatgaacgttgtgtagaggtgtgtcttcttcttcttcttcttcttcc
actcagggttttaggggaggtgatattctatatttgggtttgggtctgggtactgcaacactaggctattaag
atctcatccttactgctttgccccctcctatctttccagaaacccacaatggatttgctagaaataatgggga
gtcctgtttggacaggatataaccatttctcagctagaggatattgttggaaatgaagaaagataaatgggga
gaagggaactcacattgcttggcacttaaatgaagccatgtactgtgttgggaaattatttatattatctc
gttgaatccacagtagaacaacaggtgaacaccatacaaggtaagtattgtcatccttattttaccatgagga
aattgatgcttagagagcataaaagccttggccaggggcacatagttgggaagccggggctaattcatgctg
ggctcttctgatagttttcttttttaattgtccctcctcattgttaccttggggatttcaagagattca
tgtagcttctaaatcaacgaactgatctcctggagagcagcttctgtatgagaaaaatctagctaattattta
ttcagtgctctctggaaatgcaagctctgtcctgagccacttagaaaaaacttgggatgacaagcatgtgtc
ttacaattgctgctctgggttggcagtgctgtgctgccagttgtcatcttgaacaaactgatgcagtgctggt
ttaactcttctctttttggagtaagaaacttggaggcctgtgtccttctagaagtttgctgagcaaatgg
taaggaaaaagaaataggtcctaaggcttgactatttcagagaaatttcttctcagacactgcaatttctccaatctcttgactttt
gaattggaatacatagtggtaggtgtcttcttcttctcagacactgcaatttctccaatctcttgactttt
ctagaagttttaatccaagtccttgttgggtgggtzagataaaagggtattgttctactagagactgacctg
gcatggagatctcatttggactcacagatcttctagctcagcgttgggtttgtatccatacctcgtcactgc
attcttagttccttctgctccttgttctcctcatgcccagtgctccaccctacccttggccctactcctctaga
ggccacagtgattcactgagccatttcataagcacagctaggagagttcatggctaccaagtggccagcagg
ccgaattttcacctgtgtgtcctccttccatttttcatcttctgccccctccccagctttaactttaatat
aactacttgggactattccagcattaaataagggttaactgctggatgggtgggtgggtatcacagaatgtag
tatcccttgttcacgagaagaccttcttggccctagcatggcaaacagtcctccaaggaggcacctgtgacac
ccaacggagtagggggggcggtgtgttcagggtgcaggtggaacaaggccagaagtgtgcataatgtgtgacca
tgggagcttgtttgtcggtttcacagttgatgcccctgagcctgccatagcagacttgtttctccatgggatg
ctgttttcttctccagagacacagcgttaggggtgtcctcattacctgagagccagggtgtcggttagcattttc
ttgggtgtttactcacactcatctaaggcacgttgggttttccagattaggaaactgctttatgtatgggtgc
tttttttttttttttttttggagacagagctcctgctctgtcgccatgctggagtgtagtgacacaaatcctggctc
actgcacctccgctgcccagggttcagcgttctcctgctcagcctcccaagtagctgggactacagggtgcc
tgccacctgcccagctaatttttgtatttttagtagagacgggtttcaccgtattggctaggatgggtctc
gatttcttgacctcgtgatccgctgctcggcctcccaagtgctgggattataggcttgagccaccacgc
ctggccgatgggtgcttttatcatttgaaggactcagttgtataaaccactgaaaatttagtatgtaagggaag
ttcagggaatagataaagtcactccaggcttgaggcaaaatttacaatgctgctgactttgtatgtaagggt
gaggcattttcttagaazaagzagaggtaggctctctgggattccagtatgccatttccatcctcagtggttt
tggccacctgagagaggtctattttcagaaatgcattcttccattccagatgataacatctatagaactaaa
atgattaggaccataaacagtagctcctagcctgctgtcggaacacctcccgagtcctcttgggtggaa
cccagaggctgggagctggtagctcatgatccattgagaagcagtcagtgagagctgtgtgttggagggt
ctcagctgagaggggtgatttagcagtcctcattgggtgtatggcttgcagcaataactgatggctgttcc

cctcctgctttatctttcagTTAATGACCAGCCACzGGCGTCCCTGCTGTGAGCTCTGGCCGCTGCCCTTCCA
GGGCTCCCGAGCCACACGCTGGGGGTGCTGGCTGAGGGAACATGGCTTGTGGCCTCAGCTGAGGTTGCTGC
TGTGGAAGAACCTCACTTTTCAAGAAGACAAACAGtaagcttgggtttttcagcagcggggggttctctca
ttttttctttgtgggttttgagttggggattggaggaggaggaggagggaaggaagctgtgttgggttttcacac
agggttggatggaatctggctcttatggacacagracctgtgtggtccggatatggcatgtggcttatcatag
agggcagatttgcagccaggtagaaatagtagcttttgggtttgtgctactgccaggcatgagttctgatccc
taggacctgggtccgaatcgccctgagcaccctcttttcccttttggctgcagccctgggagccacctggc
tctccaaaagccctaatgggccccctgtattctggaagctgtgggtgaagtgaagttagtgggccctctct
agagatcaatactgggtatcttgggtgtcaatctggattctttccctcaggccctggaggaataataaactga
gacttgtttttatttctgcagagggttctaaagccattcacttcccagatggggccaataatgctttgagtaatc
tggagatcatcttttaatgcgcaggtgaatggaactcttccacagagggtgtgagggctgtagagcagagtg
aactzccctgaaactcagacgtcagctctttgtctctcttatctctgaacacccttcccttagagatcccctctc
taggatgcatttctctgtagtttagtttctaaagtctcttgttccctgttctgctcttattttttttctggat
tctaagccagtatcccacttgggtgtcttaatgtagcttaacatgtctgtaatacaaatgtatcttctct
gagattcaaagggtctaaaggactttggagagaatttccattcagttttccctcaaactagaataatgcttgc
actgtctgtaaaagaacaaaggtgtcaaagcatcttttgggtcactaaatttccctttttttattatagttta
cttaaatatttaggaagtzaaaagttaggtataaacttctttaggctgttattatacaactatatgacccat
acataatttacaatttaagtgcagccaaaattgcaaaatcaataccattcaaattaaacttaacttgggtg
aggcagctgttgttcaactgaaaccaaattataagttgcatggcagtaaatgctatcatgctgatcattttg
agtttggccagctctatatztatcatgtgctaatgtgaattctccaccctttttctacttgtatgacctt
aatttggatggcacctgttccatctctcatgagtttgcataattatactggtgccaacacaaatcataaacaca
aatataaaacttgggctttgaaatcttgtgcccagaacttggctttaaagtaagcatttaaaaaatccatatgt
gtttattagactttgtttagatgactgttgaatgaaaacaaagtggtttaaatacctcttagagaacttaaa
tataatccctcagcaatatgtatacagatcttcccttggagaaaaactgattgtgttcagcctctcatgttac
aaatgggggaacctgaattctgaggtctctagttagagagaacagggactggaatctgtggaztccctatctgttt
taataataattgtaaagtataatagataatattatataataaaaaataaaagcaaacacttagaatgagcttc
catgtgtgaggcactaactgatttaggcattattaacttagatttatttccctttaaaggccccgcgactgtactgt
tatttccacatgtttagctggggaacgtgctactcagagagggttaagtaacttgtctgaggtccacaccac
taacaaggagcagcaggttaggttcaaataccagataatctgacttggagctggcactctaactcaatgtgccc
taatcgcttttccagtggtgtcattattttgcctatttccatctgagaatattgaagtttctgactccttcc
ttgcttttctccctgctcccggtgttatccccaggtcttgggtgttccagtcctctatgtccgctcttacc
ttatttctttgtctacagtggtatccagggctctgccccttcttatcctggtagagggggcccacttgcgtgg
gaaattgtctccgcatggtttatccatgttgtgtgtctcattagtgagtagtgagggaagaatcatatcatgtt
ggcaatgaaagggggggttatccatgttgtgtgtctcattagtgagtagtgagggaagaatcatatcatgtt
gttacaaagcaggggaagggatttctttaggtcaccagccagcgaactgagctgcaaccagaagctgagatcc
ccaggactaggggcagcctcattctgtcccatcacagtgaacttttcttccctcctccaaactatttttatt
ttttatttttttgcagctgcttagcagcttgaagtttagaagaaagggcagggaaaaaggttttccgtgcttag
ccagggaaggaatccctgcaacaggatgtgggggtgggtcattcaaattggggcagactccactgggtcttgtt
gcttcttctgcttgggtattgcagatgggtttaaaagtgttaggattagagagataggcaggtttagccaaaggc
agttttagccttgtggcagagttctttttaaagaaggaagtgggatgcaacaccctgacacaaaggggctt
aagttgttataccactgcctgctaacctgttttcccttaactctcttccctgatttctaaaggaagtattttt
gctgaatcagaaagaaaagtgattttatttccaggttgcgtgattgcttagattgttagagttggaagatctggc
ttgcatcttgtacagctgacagaactggggctcaggggggacaggtgcccagagttggctcagtcaggaag
tagcaccagaaccagctctcctgggtggcctacagttgcagacccttttttgccttgcctctctgtgtatacta
aagcttctatgtctctgaatctcaagttctgactggtagctactttccaatccacctggcttagatttctag
attatattgttttagacgtcagaacctctaaagggttttggggccacttggtagctcacatagtgagaaccag
ccctgcccattaggttaggggaagaagtttagcagctccatgatagctgttgcctgcagcgtatggatgttccatt
gcacagttcctgtctcctgagatcctggagtgatacgttggcctcagagccagcagagcctggccct
tgggacatgcttagtaagttattactgaatgagtgaggaaatgtcttaaggcccattagtttgcaggtcttga
ggaggctcccttgcactaggaagaatagaaagcacaataagcctgtgtgctgcccaggaagactagaa
acgttatgttgcagcctggagctgaatggtatacccccagagcaaccctgttgaaaggcagtgcttgccttttc
attctgtgtcctgggtttgtggttaactcctgggtccccctgctctcctgtacccccattgtgcagactgagg
ggggaccatcagccagggttagttttccgctgttctgttaggcaaaagaataaattgaattgagttgtgaaa
gttgggtgcaaagctcagtttgggtccaaagttaacagtttaacttgtgtgggtggcaggtattcagttcaaac
agggtgggggacaggaaggggaagagaactcagagctttcagatcctcatctgggttttaggtgatccag
aggccaaggtccccatggaacaaactggacaaagtggaggtggccacatggcctcttttcttttgcctttat
tattaattttctcaaatagatctgactagtcatgtgggtgggaaaatagtttaattgtgatttttttttttt

aaactgagtcctactctattgcccaggctggagtgagtggtatgatctcagctcgccgcaacctctgcctc
ccgggatcaagcaattgtcatgcctcagcctcccgggtagctgggattatgggcacacagcaccacgcctgg
ctaattttttagtatttttagtagacatgggttttagcatgttgccaggctgggtcttgaactcctgacctca
agtgatccacccacctcagccttccaatctgctgggattacagggcatgagccactgcacccagccagagtac
cactatttgggcattctttaatgaaaaagaatgaactatccaaaaattaaaactcctcatttatgagctttt
agagaattttacagagtagatggaaactctctgcaccttccccacttctagtttcacctgacacatttct
tccctgtccttactcctggggccggcagcagtggtcatgattccaatcccagcttggccaccatctgcctcag
tggcctagggaaaactcctttctccagagcttttagttttctcttctacggaatgaagaaagttaaaacaaata
gacatttattgtttcatttggataaatactatttaagcatctattacttgtggtatgggttagctgggtatat
agtggatgaagcagctgggcatgagtactgctttcgtagagcttacagttcagtgaggccagcagatgtgaaa
catatcatcacacaaaataaaaaataaactatcaactgtgatgaggattatgaaggaaaaaatccggcaaaact
atgggtactgggttagatactagcaggtgtgggttagggatttctatttagattgacaggttgtcacattaaag
ctgagagccctgaagttcaagcaatgggttagccaggcaaaagatcagaggcttagagatagggaaatccattc
caggcagagagactgggggtgcctgtcccttaggtcagggaacagaagaaagccagtgccactgggtggagt
aataagactggcgggggatgagttggtagtagacatgaccagatmatttagggczcaattctcctcggggza
aggagaattztaatttaataattttattttattttattttattttattttattttattttattttttcaa
gacggagtctagttctgtcgccaggctggagtgagtgagcaatctcggtcactgcaacttttgcctcc
tgggtttcaagcgattctzccctgcctcagzcctcctagctgggtattacagacgcccaccaccatgcccag
ctaaazttttttagtatttttagagatgcggtttccacatattggccaggctgggtctgaaactcctgacctg
tgatcctcctacctcggcttcccaaagtgcgtgggtattacaggcgtgacccacagtgccccctgagaatttaa
ttttattttatgtgcaagaggattccctgaggttagtcaggccacattgtctgggtgactcttgggttagaggg
aacttgaatgacaaaggcccaagaaagcaattgttaattacatatatagaggtttagtattttagctgtttt
ttctttcatttaacattatttagtggtgcgtgttccacatatttctaaatcatcttctgatttagaataatgat
ttctgattgtgtaggctgtgtttttatagttttgaaagtaataactttgatattccattacttztctgattctca
cagcaattctgaggtgtatgcgttgcaatttctgtttcacagatgaagagagttattgttaataagtttaattg
gcccggcatgggtggctcacacctataattccagcacttggggagaccaaggtgggaggatcactgaggcca
ggaaatttgagaccagcctgggtcaatgtggtgacacccatctctactaaaaatacaaaaattagccagcggtg
gtagcacttgccgttaattccagctatttggggaggggtgacagagcgagactctgtctcaaaaaat
agttgcagtgagccaaagattgcacacactgtactcctgcctgggtgacagagcgagactctgtctcaaaaaat
aaaaagttgctaagaggagggtcgggatcttttggctccaaatctactgtgggtgatgacctttgacattcc
tgatagctgtgcagtaattccattaacacagttttataagttcaaaazccctgttgcccaacatttagattgtt
ccatgtgtgctgttacaataaattactataaagattctatacatattaatcttttattattttttagtattt
tctgtgagccaaaatctgaggaacaggattactaggttgaagggaatggcccttgaagtgctctgatcagat
gtctttccagaggatccaaccaatttaaatagccaccatcaatgcagagactttgtagttcagggaaggca
ggcctgggttttaaaaatcatttccctctctagcattttctgtatgtgatccttaagatttcaactttagttt
tcccagggtctcattggcatgtatgctgttagggatgggtctaaaaattaatttttcttccacattcatatcatg
tcacccagtgatttttaataaataatcacttgatttaaatagtgattccttttctagttatttttgggaca
tttattaaaaacctggatattgggtggctcatgcctgtattcccagcacttggggaggctgaggtggggggattg
cttgagactaggagttcaacaccagcctgggcagcatagcaagactccatctctataaaaaataaggaaatta
gtcaggcatgggtzggtagtgcctggagtcacagctacttggagggtgaggtaggagaattgcttgagttcc
aggtgggtcaaggctgcagtgagctatgaccatactactgtactccagcctgggcaacagagtgaaactctgt
ctgaaaaaataaaaaaazzzzzzaaaaaaagatgtgtaggaggcaattttggagttat
tcatttgggtcatttgatatttagtttttagttttgggtgctgatagagcccagaatgtaccctgaatttgatga
acattctgatattgggggagctcatgtccccacttaccttttgcctctcagaatactttttgatattt
ttatctgtttttcccccattgaatgttattaccttataagctcaaaaaagtagccctatcgctatttttaagt
tcagttgtgttaaatctataaattagcttgggaaatttggatattaaatgaactcatgaagaagcagagttt
agctctccttaatttctcatcttctttattttatctactacagttctgtggttttcttttatgtaagaagca
catgztttggctaagttaatgcctaggttttttggttatgtgtccattctcactgtggatagatttctctt
ttccccacattatattaatttaactgggttttcagagactaatagcaatgctattatttaggagaatttacct
tgggtctgatttaacttaccatacttgcaaatcatttgcagcttttttagttaactttgtgagttctcttaga
tttacgaccatgccagaaacagaaaggatatttcatctcttcttctgtatgtttattcttctgttttct
ttttttatccccattatattctcaagaatctctcaataactaagaaatagcgacttatttttcagcgzcg
agtgcattattttggctaccatgattcagaagcctcttgccctaaaggcccaattttattctgtagttttctc
tgttctttgtacatggcccttgccgtgccttaacctgaattaacgtggctaaatctcaagaatttaagagc
accgtgactgtgtcctcaggctagggaaggaaatgggttcacagagtgactggattgtgggtctatgaacttc
ggcagccagcaaaagtcaggcatgaataatcaagtgagcagtgaaacatctgtagtggtggagatgttgg
cataactatgaatgatgattcaagagtggtttgatgcattatgaataacatgatgataagtagactctg

tgctaagccttctatgtgaaatacatttaattctcataataactctagagcagtggttctcgaccgggggcg
attatcccccctagcccaacccacccctcacccttcaccagggacataacatctcgaagatatttttqatttc

ttctcttgccctggcctcccaagtagctgggattacaggcatacaccccatgcccataatttttgtatt
tttagtagacacagcgtttcactaaaattttgatttttagtagagatgggggttcaccatgttgccaggc
tggtctccaaactcctgacctcaggtgatccgcctgccttgccctcacaaagtgattacaggcatgagccact
gcatccatcgccaaaaagattttttaaagaggtttaatgtagaacatatacaaaggtctttggaaataaaaa
acagttttttaaataatcagaaataaaacaacaaataaaataaaaaacaccccaaaacaatctgaa
gcacgagcacctagcagaaaaggttcaattatgatctattcatagagtggaaatatcaagtagacattacagga
catgttttaagattatattttatgtcatgggaaatgctctccagtatgatgttaaataaaaaacagaata
caaaagtatatatgtctgcatagtctcaatattgtagagaaaaaataattttatgtatgcatgaaaaagac
aaaagatgttaacagagatccattgttacttcagtttactagggtatgtctctgggaggttaggattaaggtg
atttatatttactttttaaacttttctgtattttttttttttttcaattttccataaaaaataaaggttg
aagatcaagaaaaaatttctgctttggctcagtgagtggtcacgcctgtaatcccagcagtttgggagcc
ctaggggagaggatcacttgaaccaagagtttgacgttccagtgagctatgatctccggatcgtaaccgct
ggacgatggagcaagaccctgtctcaaaaaaaaaaattcttgcctttttttttttgtttgttttgagacgga
gtctctctctgttgccccagctggagtagcagtgccacaatctcagctcacccgaacctctgcctcctgggt
caagcgattctcttgcctcagcctcccaagtagcctgggattccatgacccaccactatgcccagctttt
tttgattttcagtagagacagggtttcaccatgttggccaggctgggtctgaattcctgacctcagctgat
ccaccggccttgccctcccaaagtgctgggattacaggcatgagccactgtgccagcccaatcttttgctt
tttttaaaaaagaagacaaaaagggattttataccagttatcttggctgtgtgactctgaagccacagt
tgtaagttataattactctgaacacaaagccctgtgactctttgggctctttgggtgtttatcttgattac
aacgttggaatatagaaatgaaggaatgggagagtgatagacttcaggcagtgtaactagttgtctgaac
actactggctcaattatattgtgtctagtgtatttccatcttgtccgtctgctaatttatcgcttggttaactc
actgaggcaggggttttcttggagaaacctcattgttttaaccagtgatcatgcttgtttagaagttcaa
tgactcttttaactcatcggaagatgatgaccagacctggacagatggggaaggactttgcaactctctct
ttacagtgctgagtgcacacaggtcaatatgggaactatgtgtgaattttcattgtctttgagagccctcttc
tctgccccataggagcagctttgtgtgcaattagaggagcaaggggtgtgtgtatttagcacagcaggttg
gcctggctctctctctcaacatagtcaccacatacctggcactatgctaaggctgggaatgcagacagatg
ggtgcctgctttcagagtgtcaatgtgtgaggaagccagcaacagaaacagatgatttcaggagctccag
gaaaaatgctacaggaggagtgctgcctgggttactggagtagcacaggaggagggttctagctcaggctgag
atttttagtaaaaggaaattatgccacgatgaatcctgaagaatgaatagaagtgaaccagataaagcacgata
ggaagcatcttcccttacctaagggaagacacagaggtatatggaatggtatgttaaaaggttgggactcca
aacagttctgttaaagcttagagagtggtgggagagactggagaagttgat taattagtaaatgaagttgtc
tgtggatttccagatcccagtggttgatatttcaatttttaaaatttacagtgttctatcttattt
cccactcagTGTCAGCTGCTGCTGGAAGTGGCCTGGCCTCTATTATCTTCTGATCCTGATCTCTGTTCCG
CTGAGCTACCCACCTATGAACAACATGAATgtaagtaactgtggatgttgccctgagactcaccaatggcag
ggaaaatccaggcaatataacgtgggctaaattggacttttccaaagatgctgtctttgggaaacatcacaca
tgctttggatcagzaaaacctaggcttctaatttgttgataaggcatgaactcaggagactgttttcagtc
tagtgaatgggtgataattgttaattataacagtagacacacatctcttttacacattttaaatcatgaaatag
aataaccttactgataattttagaaagtggtgattaaaaagcacatttaagataatgccttaaacacctagtct
tttccatagcatgatgtcttaatacacacattgcaaatcatggaacacagaattttaagcagcattttgtgta
gaacttctcagttttactaataattatttttttttttctcacaacaccttgaaatagaactcagatcatctg
tcaatcatgtattttgataacagcctttacagttagcatagaaaatacagttagtggttaacaacacaggctc
cagatgtcaggttatctgggtatgaattctgggtgtcagcatcactaagcatatgaccttggacaagtgtat
taagtttcttttaaacagagaatagtaataacctacctcatattattattgtcagtgatcatcttacaatca
cagtccttctcttagggctgggctcagtggttggttgacactgcagaaatggccagatctaaaggatcaac
atttacgtagctgggaaatgtagctgggacttcagtttactgccttagtgatttttctaccactaagcag
ctcagtcacataccctacgagaccacagcttatgagatactgttcttccaggaaagcagtggtggccaggg
ccaccttttaattgtgtttcttggcctgggtcccatctttctcacaatatatagcaacagttatttacttgct
gattttctaatgcacatcacacatagtcataattaaacacacacacacacacacacacacacacacacccctc
aagaaacattttctgagacgtgatttctctgatttcatcaaaaaagaaaagagcgggcccaggccagtgaggaa
gtcaaggtgggtggatcacttgaggtcaggagtttgaaccagcctggccaacacaggtggaacctcgtctct
actaaaaatacaaaaaatttagccaggcgtgggtggcgcacacctgtaatcccagctactggggagctgaggca
ggagaattgcttcaacctgcgaggtgaggttgagtgagccgagattgcccattgcaactccagcctgggc
aacagagtgaga;tctgtctcaaaaaaaaaaaaaaaaaaaaaagcataaactgaaatttatatgcaatttat
atgcctgtgagataattctgttttctcttttggaaaccccaaagagatttttttgattgatgagcaaatatcat
tctactagacgaatgattttctggaatgattacaagcagggcaazgatgggtgzztagtggaataagcaaatgt
cttcggcatcagacaagttgggggtttgtttgtatcctgcctctgccttcaccgaggttgtgatcttgggca

18/86

gtgtggggagccatgggagtggttagggccagcctgtggaggacctgggagccaggctgagttctatgcac
ttggcagtcacttctgtaaagcagcagaggcagttggcctagctaaagcctttcgccctttcttgcacccctt
tacagTGTGGCTCGCCTGTTCTCAGATGCTCGGAGGCTTCTTTTATACAGCCAGAAAGACACCAGCATGAAG
GACATGCGCAAAGTTCTGAGAACATTACAGCAGATCAAGAAATCCAGCTCAAGtaagtaaaaaccttctctg
catccgtttataattggaaattgacctgcaccagggaaagagagtagccagggtgtctggggcttgttccca
ttagatcttcccccaaggggtttttctccttggtggctggcctgtggggccctctccaggaggcatgtgtga
agaaactaggggagctgggtggccacagacagtgatgtactaatcttctctgggaagacagaaaaggtccc
cagggagaatactacagacttggccttagggacagctagggtgagattgctgccaactgcattttttct
gaagtggccatattggttgagtgaaatggatttatagacagagtagttctgtgcatataagagcaattacag
ttgtaagttgatattggataagtgaaagtttaagcacttcttctaaaaagagaatgcaattcattttccctta
atcatttcaatttagctgagtggtggttgaacttgtgtctttaaagagtgaaatctttacctctgatctg
gtaagtatccaggcaatttctgtgtgcccaccaggaggtatctggggagtggtggttctgactgaggca
ttggctgcatagcatcagagcagccttccaggcagtggtggcaaggggacagaggctggtgggagcagc
tggctgagtgagcagcagtaattggcatgtgcatggtctgtagagaatgtagaagcaataatgaagccgataaa
agctggtctgcattttattattatcatgcgcgggtggttctaaacaatgtcagtgataaattactcctccccc
atcatggaccaatggctggcactgctccagggaagtgctttttattccgttgggtgtttaggagggtatgga
gttggctggcctttgctgaaaggcctaccagtttgttttctatttggcaaaagaagaatgataaagtttyta
gagtttaaaccagactcagatttgagtttttttttttttttttttttttttttttttaaggctacagaactgtg
ctttccttgggcagtaaaagaggcaatgggcaatgtgggacctgatzgacaazagggaazzzgzzzzczzaz
zzazzzzzzgctgtcttaggggtggcatggaggagtgctgtcttcacagcagagagaggtatggctgtgctt
ggagtgtccacttagacaactcctggctgtgagccaggccatcgagatgctgtttccttgacctgcaggtc
ctggctctgcacatggatgtttcttctggtgcaggagacagaaaggtagcaacaacccctgatcaaagcctc
agtccctccttatttactggagagccctgctgattgaccagaggcacagctggggatatttctttacctc
tgtagcaagagacagcgtggtgcagaggaaagtgtcagcatacattaccctgtggctgcagctttgtgaa
taggtttagtagcacctttcagccacttcttcttacctgttaattgagataaaaacatgtaattgcttaaaaa
cagttatttggcacataggaagcacttagtgaaatgaattatgatttttttggagtgggtgacatctcaacc
aagccatttaacccctcagccttactttcctcaactataaaatagcagctaacttgaaatgtaaaactataa
aacctaattgtagtatctggcacatagtagattcccaataaatgagagccagttattctttctaagacagtgat
gcatttctgagcacctggccttgttcttctgcttgcattttagtcagcagttgaaatagactggctgatgg
ggtaagttgtcaagcagactttctgatcttagtgaggagactgccttaaaacaacactaatttctctttt
cttttcttttcttttcttttaagacagagcctcgctctgtcaccaggctggagtgcagtgggcagctcttg
ctcactgcagcctctgctcctgggttcaagcgattctcctgcctcagcctcctgagtagctgggactatag
gcatgctccaccatgcccactaatttttgtatttttagtagagatgagatttaccattgtggcaggatg
ttctcgatctcctaaccctgtgatctgcccgcctaggccttccaaagtgtgggattacaggatgagccac
catgcttggccttctttgagaagctggagacatgagtttaagtggtgaagaagccaaatctgtatctaaaaac
cctacagtagtggtgcagagctctgaggagagaaggtcccttagattttgagtgattattatgtcagtgctt
gttttacatctctctgttcacgcagtagtgccttttctgcttgcagctgtttcttaaaattctttcttct
ttgtctgtcttgcagcacaacaggccttcagtagatgggggaaatgcacagaaacactgccttttctaca
ggaaatcagtaacttttactgattttgtttttatttacttattttatttgttttaaaattatttttagtttt
tttttttttagagacagggtctcttctgttaccaggcttagagtgcagtggtgccccttagagctcactga
gctcactgcagcctcgaattctgggctcaagtgatcctcctgccttagcctcccgaagggtgggatgaca
ggcatgagccactgcacctggccaacttttctgtgattgcgaatagcactcttgtaatttccggagagaagc
tgagactggcatatgtcagtaggtatccccacttagagacctgtgtttatctgcactgacaccccatcacag
catgatgagcttggccctcctgtgctgtctctccagggtgggaggatccttgaagctgatctggtttgga
gctttgtcctcattcacctcctttaccacacacccaccttcccagggtggggatctaccactcactaagtag
cccattctgggtgttgacagctctaattgtttagaaaatattcaccaccctgttatgtttcttagagaacaag
tctaattctgttttcttctgaaatagtcgaagacagctctcatgtttttcttctcctgttttcccaaggtcca
tgatttttttaggcaaaatggcctccttctcttattggaatgttttctcctcccatcttctgctctcctctg
gttgtgtttcagtagtctgtgtgcttcttgaagtttactggaaattatgaaagtattctggcacagaggag
gaagggtttttgctccttgttctgagtgctacatttccgttaatgcagctctgagattgtatttaggcatt
ttggcattcacgtcaccttgttgactcatattccatgtgcactcaacaaaaattgtgattttttaaattagg
cagaattgcaagttacgtgttctcatttcttctgtgtattgttggcttttgaactaaagggaataatgtc
tttttctgtttttacatgttttagattccctatgc:atcctatcctcccaaaaccatttttagattctgatttt
gccatgtattatctgatactccttctcgtcatctagagatgtgataaaacactctcttggcctcattc
cagtcacgataactgtgggacaaagacttgaagcttggatcagtcagtgaggactaaccacccctgtaga
cccttttttctcactataaaatagcagctaactgaaatgtaaaactataaaacctaagttagtatctggc
acatagtagattcccaataaatgagagccagtagttcttctaagacagtgatgcatttctgagcacctggcct

tgttcttctgacctgcaatttatgcagcagttgaaatagactggctgatgggggtaagtgtgcaagcagact
ttctgatcttagtggaggagactgaccttaaaacaccactaatttccttttcttcttcttcttcttctt
tttttaagacagagcctcgctctgtcaccaggtggagtgagtgagtgagtgagtgagtgagtgagtgag
ctgacctctgggttcaagtgtattctgtgtagactaccactcaggcctatattgtaatcagtgctg
ggcactgggctcctgctctgtgatccagttgggaagtttatctgttcttccctcagcttgcatctgct
aaattcgctggactatacacaggtgattttagatagtgaggatctctactcaaatactctcatgatttctt
ggctagagcatcattttatttccacttatttggaagagaccttagagaccagttagttcatttatagataaat
tagttgattctgtcattcaaccttatatataggcgtctcctatatgcgaatcactgttctaagtgcag
acacagaggtgtccaaaacaaatatggccctctccatatggaatttctattctagagaagaatctgacca
gaagggggaagtgtgactgtcccaagttacacaaccacagaagggtatattctgggaataaatcacggctaaac
ccccctgctgctccaggcagttctcctctacagtgctcttatgtgctgttttaataatcttccaactggga
agaactccccatttcaggaattaaagccgtggacaaatctttaaattatccttgaaatcatcctaataagaaat
caaaggaggaagtcttacagggtgctcaccacttttctcatcactggaacttttagacattttattatt
ttcttctaaaccagagtacaggcacacaagttgagtggtgtggtggctaaattaataatgtttgcaaggc
agtgtgagaagcattcattcatcttaatacctatggtagtgcactcagatgtaaaaaattggataaaatcc
tcagaaaccctagggaagtgacatgtctgtattttgtctctgtgagatacagactggcagagataagtgtt
tctctgggtgagttttgtggtatctgggatgatttttaggcagtagtggtgagaacttttaatttaac
ccacatccaattgcaatttcatggaaattattgcttaggaggtgttcaacaggaaaaatataattaaagt
aattcaaaagaaacattttctgtgaatatggtaaaactgtgtgagagtagtttgaatatgattgaagattgga
aaacattgggtataagagtgagtggtgggttttgtattaaagattcattttgggaagaaatccatgctgcattc
ctcatgaagtgtagaactttggcagtggtgtgatttcttctggccagagttacctgaagattagctgcct
gaggtcactgagcattaaattagatgatgtctgtggatgactgatagtgaaagctcatagcccacagttgac
acataataaattcgagttgctttgcttccccctctgttctgtggtgactgtttggcctttgcccactgttctg
gcctctctgggcttaagtttcttctgcttgaaattggaactttcttgggtgaaacaaccagaaatctctc
agcccagaaacttggtcagtagtgggtgagtgactgggactacccaaggatgtgggtgtctgtctgtag
actatagcccccttgagggcaaggtgggctgtctgtcatggttccatcctaagcccagcacagtagtgggt
gcatggtgagccattagtgaaatcttgtggaatgaaggtgggagaaaaataaaatacctgtacttcacagggt
attgtgaggggtcaagtaaaagtgtcttaaaaaattgtattatagtttattccctgtgttagcccaggtc
aacagagcctacgaataataatgatgacagaagttctcaaaaagcttggccttcttcttcaaaaaatt
gccccccagagctttctggaaggcagccatgaaccagagggcctaaagtagatttactgggaagctaaaaa
tattactttatttttcatagctccttcaaggtcctctctgggggtcttagcaatatgtttacacagtggt
atgtttttgtaaggtttgcaaaagtaagattttttaaataactatctgtttttaaagagagccccctac
caactgtgtcagcctcaggccccccactgcattctgctcctgccagggtcaggtggggcaagaagcactgct
ccccctccaaagcttcccttcttgccctggagtcactcctcactccccactccaagccactgcatcgctgt
gccccctctctgggtgaatctggcattcttaggtgggtgagaagcagactggcccaagctaaggcctttctg
atggggtgtgtgctgctgagaatcatgactgggtgggagaggaggtgacctttzgtgtcttatttttac
tgtgtatttctttttagctactttaaattgtattgcttagtgatacctaatgggttcattagcctgctcct
actgaacatttccgctcaggcatccacttggtcccaaggcctgctcctctcccatattctgaaattctggact
acagactctcattcaactccaggttgcaactgtggacacagttccctcttgagcaggtacctccttgagtggt
ttgggacgtcctacttggtcattagttgggaagtgcatatgctggagctgaagcctcttgccctcccgggat
agggcgctcctcacatccccctctgagaagttccccagcttccctctgttccccgtttccacacttagcgaggc
totgttccactgctacatcccccatagccagtcctcctcagccttgccattgcttatgctggtctggaacaat
tcctagactgtggggcatctggggaagttctccatttctttagctggcatgacccaagtggtgtgggca
gggtctgtgattctatggtgtgggtggaagccaggtagcctctctctactgtacatggaactcagcaacttc
tgagtcaagcaagatcttagctctgcaggtgtcttgccctgtccaaagttatggccacaccagtagctttta
actctagaagcccagtaagtggtttgtgggaccgcaagatcattttctagacctgctgaatatgctctagaa
cgggttagggatggctttcagcgtgttcttagggctgacaaagtacacagtttctgggggtacatacacaccgc
ggctccctgtgaatggcactctccatgagaactgtgatttgagttgaatagtgacagcctacatgggttc
tctgccatggcctggagttccttatcttgccctctccagtgaggactagggctgcaactggcctactttggc
tccctgacttgggggtattctgaaataccttttttttaaggttggtggagctctctgaagcttataaggattt
tgccaggaaaagataagaaatatctttgggcattttgtcactgtgctggagatgaacctttggaggacata
tcacctgttgaggtcaaggggcaagggacaggactggcagaagatccggggcagcagcctgccatcc
cgactgagtagtgagtttctctctcctctcagctgcacttttggtggagtcagtggtcagctgccacttc
ccttatgttcatggcatgaatctggctgttaggcctttcttttttttttttttttttttttttttttttt
ctctgttgccaggatggagtgcatggagtgtagtggtgtgactctcggtcactgcgaccaccgcctctctg
attcaagcgattctctgctcagcctcctgagaagctgggattacagggcgatgccacaacaccctgctaa
tttttaattttttatt

tcctatgtctacttctttctacacagacacagcaacaatctgatttctctatcttttccccacatttcccc
ttttctatttcgacaaaaactgccattgtcatcatggcccatctcaatgagctgctgggtacacctcccagat
ggggcgccggccgggtagaggggctcctcacttcccagaagggggcgccgggagagggcgccccccacctcc
cggacggggcggtggccggggcggggctgccccccacctccctcccggacgggggtggctggccggggcgggg
gctggccccccacctccctcccggacggggcggtggctggccctgctaatzttttgtattttcagtagagatg
gggtttttaccatgttggtcaggctggtctcgaactczczztzgacctgttgatccaccztgzczctcazgc
zzctcccaaagtgttgagatztacaggcatgagccactgcccggctctgttzttttggtttggtttgg
tttttggtttttggagacggagcttactctgttggccaggctggagtgagtgaggcgccacgatcttg
gttactgcaacctctgctcccgggttczaaacaattcttctgczctzcagcctcccgaatagctggga
ttacazggcacttaccacczagcctggctaatttttgtatttttttagtagzzazgacgggggtttgczcat
gttggccatttgaactcctgaccatctttzgaactcctgaccatgtttgczcatgttgaactcttgacttca
gzgtgcgttgggccztcccaaagtgtgggattacaggtgtgagccaccatgccagcctgttggcctttct
gatatzgzczctcztgactaatcttttggaaattzagzztccccagggttatactggattttacttaggg
aaaagggtcatgczctctctggctgtcagzatttactgatagtaactaaggzactcagztgggggtgzzgzac
ctttgattczztzggtttgatttttggaaatzcaaaaagacgtgagctccaggggagcagggtggctttgggtg
azcatggcagaatagttggctgtggczagggagtgagggaagtgggtagaaaaattaacatctgtazaata
tttzzczctgggaaatatacctctgtgttaagagagacagactggcgagzczazzzgzazzztzzggcc
taggttcaaatcttggcttgatgcttatcagctgtgtaacctggataattccatcacatctctgtgctcag
tttctcaaatggaataacaatagtacctccctcaggactattgtggcaaatataggacgaataaggggaa
gcacttagtacagtgccctggcccagcataggtaccaggctgttcttaagctcactgcattttacaacat
cataaaatgcaggggatcacacacatgaaggagccgaagttcagagaggccaagtaacttgcctaaagca
cactgggcaaggggcagtaataggaccagaattccagtttctgtgctctgttgttgttatatcctaagag
agcagctctgagtagccagaagcttccctaaagtcacaggacatggggcatgggtggctgggatgagaaag
gagacaagaggggttctgaaagaaatgccagattcactccacttctggcttcaggcacccgatggaatgtt
cccaaggcccatctagaaagaacatcctgtgtgactcagccacttctcattttctgtctgaacccccacc
cattcaggcagctgtctaaagttaggttacagcctcagctatatattttctgtccttgtggaacccccagtg
tcatcttgttgggagatctggtgatacatgtgtcaacattatgtcatcaaaatggaaattctttgaaatctt
taggtgattgcaattcacgttctgtatgtatgcacttgtcaaaagttttgatttgaggccttagaattttat
atttggaaaccttccactaccatgagttttcccagacctgtcaaagccaggctgcacatcagaaccagggt
ctttgatttccatccaggggcagggtcctgggcccagctgggctgtaagcagggtgggggtgggagcaacgct
gcactgcaaatgttgaaatattacttgaactaaatcaaatcaaagatcagctttactcagacaagaatagaaa
acacaattgcattcgattacagaatagtggttatccccacaaatatcagactgccttcaaaaagttttgaat
tgtaacatcaagaacagtggttgcgtgtctcctgcttttccagcataagggttattttacttgtgggtggca
aagagcaatttgggagtcagtttgtttctcattgaaagcttcccatttctggtcctctgtcactgttgc
attgaggcaccaaaaggcaatctcagtgccgacactattcaacagactaagttgcaccggataatgatccat
tttacatttttcatatattattacattgaaggcttcaaacagcactagcaggggcaaatgggtattattatc
tccatttctattgatgaggaaccgagggtcgaagggttaagtgtctgttgcgaagattaaagagtaaagttg
tacgttgaatcggggtctgactcctaggcttagcatttttccccacactatgctgccatgttcttattcc
aacattaggaagcataggtgccatccccagcttttgaggccaatatcacgatgaagcatttttaaacatct
cattaaattgctgatatagttggaagaaccaaagctttgcagtcgaagctgttgggttcaaatttaccact
tgtttgttctatgacctgagcaagatattctccagatctgttttccctcatttgaaaaatgggaataataa
cgtttctttataggctgttcttaagattctggaaaaataatgctaatagtgtgcctaatgcttggttaaat
gagtcacttttctgtgcccacaaaagcactactatgtcccttaataaattttgttaatttttaaaagttagaaa
aaaattaaactatttatacattgtgtatgttaattcttccctagaccagccttaggaagaatctcatcccca
acttgtaaactcatctttttccgttcttttgtgctggacttctcaggggccctgcaggctgattctagtcc
catgttgtgtgtgttgaagtgctgggtccctttttcagtgagagaccagctcatccttgggaactgaat
gcctcaaacctctcttttcttttctcttcccttctgtttagtgtagtcttctctgttctggactctgt
ttcttcatacttctcttcttacttcttttcaactcctttgtcttccagctgtcctctctcatttttctg
cctctcagggtcttccaggtagagttttcatctcagctatcttctgtcttttctgatgttgggtctttgttct
ttcttctcattctgttcagggtccaaaatcatttgggtcaatgttatgtcttaggttatcttccatttctc
tctgagcttcaaagccaggctgactgtgcccttcacgccttgccagtggtgaccaggacatccttccctc
tggggctgcactggctcttgggggaattgttaccattcagggtcttcaacctcttcttagggacttccag
taacttctccaccttccctcttctcagtaagacatgggtattgtcttattctgtttctgctgctagaagaa
aattctcgagactgagtaatttatacacaatagaaatttacttctcacagttctggaggctgggaatccaa
aatcaaggtgttggcaggttgggtgtctgggtgagggctgctctgcttctaagatgggtgcttgttgc
atccttaggaggggacaaacgccatttctcaactggcagaaggagctgaagcctctccctcaagcccttt
ataggggtcctcattgtcaggcctctaagcccaagccaagccatcgcatcccctgtgacttgcacatacag

22/86

gccaggcactgctggcctttggaattaaaaacccctggccctcaaggaatttctattcttctgggagcaggata
tttacatgggtgactgczagcttgatctgtgtggtagtagtggaacataggtggtgggcacaaaagagt
cacaaaacgcccggcggtggctcatgctctaatcctagcactttgggaggccaaggcgagtggtcacc
tgaggtcaggagttcaagaccgctggccaacatgatgaaaccccaactctactaaaaatacaaaaaggaa
taatagctggcggtgatggcggtgctgtaatcccaacaactcgggaggctgaggcaggagaattgcttga
acctggggctttggagggttgcaatgagccaagagcgggacacttactccagcctgggtgaaagggtgaaac
tctgtattaaaaaaagtcacaaaaagggtggccacctaaccagcttgaggatgggaaggccag
ggcaggcttctggaggaggtgactcatgggcatgtcatgaggatgggtaagaggagaaggatggttca
gacatctggcttcttaattcttggcttccaccattttctgcccagcaacataggggagaagactgag
accagcagatacaaaagccactgtactctgtcctcaccctctctttttctcccttctactaccagatc
tgagggttttgagaaatctcttctctaatatctgttggctcattcatttgggtgagaatctactatgtgcata
gcattatgaccacaaaatgtcctggctgttgcacatgagaggcttacccttctctccagccacttct
agggatttttgactctgtcctttccagaacttggctccagctgggtgctcgccatgaagcacttacagat
aaacctcatcttgggcccagtgcttccatttactgtctccttttggcttggctatctctctctgtccttct
gaattgatttgctctttatctccctttcagccttgaaagtctcgaaggcagggaactgtgtcccatct
tttctataaatggcattggtgtacattggtaaggtgagtgaaaaaatcttttgataatcacaattatta
ccatatattgagcactaccatgatgagtatctgtatcttcatactttgaaatgtggactacttacctt
catttaattggtaagaaaatttggctcagggaaggtacacttctcagagtcacagactatcttccaca
ggagagtgcagtatacaatttaggttttctgggtcccaacccctgatgtttcccccacatcattgtttctca
gacttggctgcaatcacctgaaaaattttattaaattcttttttttttttttttgagacagagctctcgct
ctgtcaccagcgtggagtgcaatgggtgcatctctgtcagtgcaaccactgcctcccagcttcaagtgt
ctctctgtctcagcctcccaagtagctgggattacaggcaccacacacactcagctaatttgatattgt
ttagttagaactgggtttccaccaggtgatctcaaacctcctgacctcaagtgatctgcccacctcaccagc
cagggttttattaaattctgatgctgggtcttaccctagcagttctcattagttgctccatgggtggcctg
ggctttgggatttttgtaagccccagctgagtgtaacgggcagtgatgtttgagaaccagtatactacac
catgttgcttctgttttccacaggttgggtgctagtgtgtgagtgtaagcctacatgggtggatctccac
gtgatcaggctgcaagttctttgtagtggaggatctttggcctcctctgctgcttcccaaccaggaacct
accacaccatgcacgtgcacagccaagggttgggtgactgtttaatcagtcctctgggttcttatgtctcatcc
gggggattcactgataggaggtggagcttgatcacatccagatgttctcatctcagagcctgttaacata
acagaagtcttataaacatgctgagcacactcactgggtctggagagtgttgaggatgacctaggcccttg
cagggttggcctgggtcgccctccacacttctgccaccctgcttgggaaggaggagctgttttgaagttc
cctgtgcaatgatgtattgtctgtctgtctgctcaggaggaagctatggcccacctagtcagtgagggtt
agctaatcagtgattctgtttctgttgagggtttcacagaggccttttttgaccttcatcttatagataag
gcagtgagggcacaaactacatgaaatgactcgacaaaataatggatttagaaccaggtttctgactccag
gggtgtgcttttccatgggtgtacagtgattaatgtctaccttttcacaccagtcctcaactgaagacacc
agcttacccttctctctgttttctcccaagaacagaaagtgaacccggatgtcgctttctgttctctgggaa
ggcagttccagtggttagaagtctgttccactcctgggggtgtggcctggggatgggtcctgacatccctgggc
tcttctctggacctggccagctaaaaggaaatctcctatgatgggtactcagataacttttggaaacctgtcagc
cctaataccatctcctagtggttagtattcagctacccttccactgggcagtaattctgtgccaggcctgatc
tgggcattgggtggtactaagaacgcataattccctatcctataggcatagtcggttagagacaacatgcaagt
aaaacaatgttctttaaactgtgggtccacacctcctcccccacattaaaagtgtagggtgcttattc
aaatgtagattttaggctctgcactctagaccactatttcagaatctctggggactgggcccagaact
gcattttcgcatgctccctaaatgaagcttaggtgctctgaggtttgacaactgcagtagagagcctaagtc
taacagtgtagagtcacatgtgatgggaagcactcaggttaggtagcagtttgaggagcactgattctgaggg
acactaaactgggcctaagaacagctactggctgtcatgaggaataactaggagctagccatagaggggtagc
agtgaatcatttctctagcgatgtaaatcttgcctcaatttattctgtctatataactcaatattactgaagt
ttgcctaaagcagaatacacctggatcatacagcatttatgagagactggctgggctgtcaggccctcctgt
tactttatctctgcatgtgacctcttasstccgggattaaactcctgtcctcattaaagcctcacactgtag
ccccattttcagatcaaacctgtttctctctgtttaaagtattcagtttgcaaggtttgcccctctagaggt
tgccttagtgctggccatgtgggtcagttcagttggtgctctgatgagctgggtttatctttattacaaagaa
gttaggctgttaggagagtgggttggaaggagaagaggttagacagccaaatgagatgagtcagggaacta
tactgtttcgaggtcatagggctcctaccaagcatctgggtcagaaacctctcattttggagatcaagaaatt
gaggttcagaaagatgacatgaggtacgcagggaagccaccagacacagcctccaactctagaactcaaat
ctctgattcttagtgctgtttttctgttttgggtgcatggattgaagccttttctaactgtactcagaggg
cctattatttagggagattccgtatgaaatccttagcaatcaaatcatttaatagggtgatgggttaaat
atatgttaatgtgttttctaaagcctggcagacctgggttttggagctttgtatcacatgttttatgtttg
aatgaaaatgagaccatgtctgtgaaggcactttgatatgcgtaatgcactctgcccagtggtttgtcaaac

atgggtccccaggtcagcagcatcagcatcacctgtaagtgtattctccagtcgcatccccggccagggmsmggg
ccmrxtctzyaggytgtgsmmggcsmggzzsggzzztgzcggcccgccggcccgccggcccgccggca
gtctgcatttttaacaagctctccaggtgattctgatgcatacttaagtttgagaaccattgcttgttttgca
ttaaacaggagatttagtctctgcagcttgtgggaataaagctttaaatctctccaatttttagctctgtgaaa
aggcagtgaggagagacaggaatgaacggactagtgccacaaagctcaggtgggggtgggtgagatcatttagaa
gagaaagaccgggcatggtggctcacgcctgtactgtcagcactttgggaggccaaggcaggttggatcaca
aggtcaggagtttgagaccagcctgcctatcatggtgaaacccctgtctgtactaaagataaaaaaaaaaaaa
tttgccagtcattggtgatgcatacctgtaatcccagctactcgggagggtgaggcaggagaatctcttgaaac
ccgggaggccgggggttgagtgagctgagattccaccattgcactccaacctagggtgacagggtgagactcc
gtctcaaaataaaaaaaaaaaaaagaaaaggagctgtgtgtgtgtgtgtgtgtgtgtgtgtgtgtgtgtgtgt
tgtgtgtaacagcaccatcacactgtttgagttgaggagcacatgctgagtggtggctcaacatgtttaccaga
aagcaatattttcatgctcctctgatatggcgatgctccccctatctcattcctgtgtgtgttttagccaggc
aactgttgatcatcaatattatgataacgtttctccactgtccattgtgcccactttttttttttttttga
gttacttactaaataaaaaataaaacactatttctcaatagACTTGAAGCTTCAAGATTTCTGGTGGACAAAT
GAAACCTTCTCTGGGTTCTGTATCACAACCTCTCTCTCCCAAAGTCTACTGTGGACAAGGCT
GATGCTATTCTCCACAAGGtaagctgatgcctccagcttctcctcagtagggctgatggcaattacgttgtgca
gctactggaaagaaatgaataaaacccctgtccttgtaatgggtgggtgaaggggagggttagtttgaataca
acttcaacttaattttacttccctattcaggcagggaattgccaaacccatccaggagtggaatatgcaacctgg
cgtcatggggccagctggttaaaataaaattgatttctggccttatcacttggcatttgtgatgatttccctcct
acaagggatacatttttaagttgagttaaacttaaaaaataattcacagttctgaggcaataaacctgggttaag
ggttattgatctggaggagctctgtctaaaaaatggaggacaggagactttagacaaggggtgtatttggaga
cttttaagaattttataaaaaataagggctggacgcagtgccactgagttgagaactgttgcttgccttgcat
aaataggagatcagtcctctgcagcttgtgggaataaaggctttaaatctctccaatttttagctctgtgagatg
gcactggggaaacagaaatgaacggactagtgtcacaagctcaggtgggatggacgagatcacttcaagg
tctgtaatcccagctctataatcccagcactttgggaggccaaggccgggaaaaatcacttgggtcaggaggt
cgagacatcctggcccaacatggcacaagcctgtctctactaaaaatatgaaaattagctcagcgtgggtggca
tgctcctgtagtcccagctactcgtgaggctgagacaggagaatcgtttgaacctgggaggccggaggttgca
gtgagccaatatcacgccattgcactccagcctggctgacagagtgagactccatctcaaaaaaaaaaaaaaa
aaaaagaattttataaaatcaggaaataatattagtggtttatgttgaattttaactttagaatcatagaaaa
cttctctggcatctattattagacagctcttgtgagtggttgagtggttgagcaccagaccagcttgcatggttat
ttttcagagacactttttgagcttattctctggcagaaaggggaactgcttctccctctctctgtctgt
catactagcttgtctttacaagaagcagaagtagtggaatgtttattcttgaaaaaagctttttgcttca
catgatctagaatttttaaaattagaaaaatgtgcttactgctgcccctctgaaactaggaaaaatagcct
tgtgtttaccaattgtgtgggttaggagatgggccaaggccatcaggcttttgaaagtagttgcatttagcat
aatttccattggccccctgccaatttccatctgtcacatctaatacagtttaaaaaaaggggcatcctaagca
tgagagatggctccttggtggtccttgaggtttctgtattttcagtatctcttttttttgagcatacaagaca
ttattgaaaaattcttgggatcaatacttgtgtgaaggaaagggaacaaagcatgattggggcagaggc
agaagatgacatcaacaaaggccctccgttgctcagattctcttttttttttttttttttttttttgagtgctc
gctctgtcacccaggtggagtgccagtggtgctgtcagctcactacaacctctgcctcccaggttcaagt
gattctctgcttcagcctcctgagtagctgggattacaggcatgcaccaccacacctggctaattgttgtat
tttttagtagagacgggggtttcaccatgttgggtggccagactgggtcttgaactcctgacctcaggtgatccg
tctgccttggcctcccaaagtgttggaaattacagacatgacccactgcaccggcctgttgtcagattctt
aaacatagacactaactgtaggctgacagcctagcagcaaggaccagttaaagaaatgagtagaactgaagt
gtgcttgagtatctctggcagtcagcaaaaaacttaattgggaatcatggtagggccaaatgttctgcagtat
caaaagctgcagtggttttgagaggcttttggtccatcactcacttaggtgttctacaagcacatcagcc
tgccccaatttaaacaggggcagttagtaatgggtgtaataaagagctctgcattgttctccttcaacaaata
ctggctataatgtttcagcactgtggatgcaaaagtgcaggataaaacaggctcttcttcaaaagcttgtg
tccactggaccacgtatgaagtagaatagtttaggtccagaaaggcaattagtaaaatagaccaagaaga
ggctctctagtgggtttggtataaagaaaagataagaatgatttagaattggcctatcaatgagataagagg
cctggctttctggcactctgctctaggggcaagtaaaatggagaattccaaattctgaaattgttagaacata
gttctgtgtcttagttaaatatctacacttacagataaaatagcataaaatgcttctcccccatttcagccc
agtcctacttaagacaacataaaattgcaaaatagtgaggatgttgttcatctataaaagtgttccagga
attcagactctggattcctgtttgccaatcatgtgtcccactcttaagaaaacaggttggaactctggattt
ttctttgcaagagggaacagagtggtggagatactgagttaatgcaacttgaggttttaagtgtcctgtca
ttgtgcttctgtctttgatacattctgagttttagtaaaagagacctgatgcattggactgttgaattggaac
ctgttttaagatcttcaagctgtattgatatgaagttctccaaagacttcaaggaccagcttccaatct
tcataatcctctgtgcttctctcttgcagtaaatgcttccagGTATTTTTGCAAGGCTACCAGTTACA

TTTGACAAGTCTGTGCAATGGATCAAAATCAGAAGAGATGATTCAACTTGGTGACCAAGAAGTTTCTGAGCT
TTGTGGCCTACCAAGGGAGAACTGGCTGCAGCAGAGCGAGTACTTCGTTCCAACATGGACATCCTGAAGCC
AATCCTGgtgagtagacttgctcactggagaaacttcaagcactaatgcttccggaatgtgaggcttttccct
tggaacagcatgactttgtttgtagaaaagtacggctggctgggagtttgtgatataattagttcagtggt
attctaatgtgttcttagtggttcttccagacttttgggccatctcccaaagggtgaaatgggaagaataagctg
gggtgtggctgagtttaagccaaaagttttttgtgcttgtttcaatcagagaagacctgctttttcatgtttt
tactattataataactaagcaagagctcatttgaaaacagagttcttcatatttaaaaaaaaagtcttgaa
accattgatgggaagatggatatctatttatgtttaaaaacccatcataaagatgacattgtgggctgtcac
agttggaaggccctggaattagatgagaccacactatttagcttacttagtaataacattgcaaagaaaaat
tccgacgaagttttttcagcctaggaatcaatagttcagagaagcactctatgagaataccattcattctt
aaccaaaaataactgggtgagcctgagcagtttgggtcatcagagtggttttatatagttccagaacaaatattgt
ctcaggtgttcttgagagctctgggtgaaattctctcgtctaccccaaacatcatcatttaatatccaggatt
ctgggttttctactcaccagatagattctcttaaaaccagggaaagattcctggaggaaggatgtatctggaa
agagatgttcttattataataaaaatgaaattgtaatactcttggattttgtgcagcagcaattctttatag
agagttgggtcctcccagagaattagaataactcagtttctggaccctgttccagatcataccctcaggtgtg
gaccttagaaacacacttcaggatttcatacctttgattgacctcaaaaagtttttgtatcggccaggtgtg
gtggctcacgccttaagtattctcagctcagcctccaggtacctgggactacagggcactgbcaccacgcc
accagcctggccaacatggtgaaacccctgtctctacaaaaatacaaaaaatagccgggctgtatgggtgggca
cctgtaattccagctactcgggaggctgaggcaggaggtatcgcttgagcctaggaggtggaggctgcagtga
gctgagatctgtctcactctgttggccaggctggagtgagtgaggcgatctzcgactcactgcaacctccg
tctctcatgcttaagtattctcagctcagcctccaggtacctgggactacagggcactgbcaccacgcc
cagctattttttgtattttttagtagacatagggtttcactatgttggccagctgggtctcgaactcctgagc
tcaagtgtatctgcccacctcgggctcccaaagtgttgggattaaaggcatgagtcacccgtgcttgggtccca
tggtataattttaagtaaggtatatttctctacagggtatcttgcaaccctaaagtaazctggcctaaag
ttagagaagctgacttggtgcagacatttgagcctgttgggtctttttgtgctgtgaaatcatagagggtgaa
aggttattatgaatggtacaaaactttgttacaaaaccattttcttggactgttttgggctgcttactgca
tgacaaatgctcaccctttcagctggaatgattgaaattttggaaaagatgggtgtttttagaagacattgt
aatttgttccgggtgctgtgcccattcattccatttacttctgtttactcattaaacacctattgtgtacac
aaccgggtaaaaatccctccactcacacaatgcctgaattataactcatagtagaatgactgtttagccctcat
catctgataattaacagctcaggtttcaacctgacagtatctctctgggaggatttagcagcgtgacagagt
cagggaatgcaccttcagaaccgtcagctacactgtgtcccatcctgctgtgttgggttgtgcttgtgg
atgctgttgggttatgaccaggtattgattaaggtggctactaccaggtgctttctgcatatctcgggttgt
ggagcactcaggttctgcttctgcccctctgctgttaccagagacctctctcaaaatggggctcttgagt
tagagtagaatgagtgatcaggattgttttgtgtaagatgatttctgagggaaggcttttaggtgaaatgac
ttccaaacattttgaaatgtgactcttacttattgaattaaagcaggcccttaattggaatgctgggactgat
acttgatttgcattaaagcagccttttctattgctgcttgggttgaaatttcaacatttgtgatggttagatg
gatgtgacatgtgatgacattgcacatgggcagttactgtgccaagaagtgcagcagtagcagcaaccgga
gatgcaaagcccaacatgatggggagagaaactcttctcaatatgtgcttctgtaccaaagtggaattt
cagagagacataattttgaaacatttctccttttgtgtgtgctgagtggtttccctgtttccagccaagggt
attgtgagtttctcctgggctccttcagaatctgggtgctctggaaagcagtggtttgggaacatggggaa
agtatggcagtggtgggagggtcagctgggtctgggtttgaatattgcatttgaatattttaccagcattgat
gtcggataaattatttagtccctgtaagcctcagtttctctctctacatacacataatataatttgactc
tttgttgtgatatttgggttacacatatgaagagcctgtgtggggcctggcacacaatagggtgctcaataaaa
tagaagttgataaatttaattgacatgagtagtagaatttatgtccttgaaaacaattgctgcaagatagaag
ttttcagccaggcagtggtcagctcagctgttgaatccagcatatttggggggccgaggcggatgaatca
cttgaggccaggagttcaagaccagcctggccaacgtggtgaaatccctctctactaaaaatacacatatt
tgccaggcaggcgtggtggcgcacacctgtaatccagctactgaagaggctgaggcacaagaatcgcttga
accaggaggtggaggttgagtgagctgagatcactccactgcattccagccagcgtgacagagtgagact
ctgtctcagaaaaagaaaaaaagatagaagttttcttctgtagatcagtggttagaactcataccaagcgaa
gtggtcctggtgagtttccagtgaaaaactgcattcttctcagatattgtcaagacttttcccccaga
ttcttattttatgtctcagtcctgaccttgtgtgaaaatttaactggatgtcagaacgctgttgtgttttta
aagttccctggggttaagagcagtttccattagggttctctgcttttacttaaaaaatcttactcatgcat
tgagcaatattttattcagttcttattatgtgtcaggtattttctaggagctggactcaactcaaaagatatc
cttttgatgagaacaaagggtgggtggatatatgaaatattatctgtgggataaattgcacttagtcatgagg
agacttgttatggagtgcgctcattgtatttgtactgttgaatttaacacttctaggaggagctcaggggca
cctggcaggggcttcttttgtcttgtgctcagcaaggtgtattttgtctgtagagtggtgctgggcaggtgaa
cttttcttaactttcttcttgggtccttctaaagcagcatgtactttcccagagcaggagagggggccactt

26/86

agtttcaacatgaaaaaagggtacagagaataacataaagaacactcctggctgggtgtgggtgggtcacgcct
gcaatcccagcactttgggagtgctgagggcagccagatcactggaggtcaggagttggagaccagcttggcca
acatgggtgaaacactgccttactgaaaaatacaagaatttagccaggcatgggtggcgtgcaacttgtaatccca
gctacgtgagagactgagggcaggagaattgcttgaacccaggagggggaggttgcaagtgaagctgagatcaca
ccactgcactctagcctgggtgacagagtgagactccgtcttcaaacaacaaacaaacaaaaagaacactc
ctgtaccatcatccatcattttgccgtgctgactccaggttctatttaagaaataaaacattacaggtacag
ctgatgccacctctgtttccctagctcattcttcagagataaactcttgccttgcagttggatgttttaatcc
tctatatcaztgtatacttacattctatgtataacaattttggactggcctaaatgtgttcacattgtat
aagtgtgcataattggcctgccacttcatttgggaattatgttcttgagatttatcaatgttgatacatgtgga
atctgggttaatttttggcatagttctatttttataactaaacttttaaaaatccatgcttctagttcttgg
cttattttttcaggttatgggtatgttttggatgcacagaaaagtaaaatlaagtcagagcaaaatctctgg
ataatccaagctttaaacttgatgtagaatttgaatcatgtgtgttttgttaaccctgtgattgcaatccat
gcttgattgtgtaactccaaccaatattcctttgaaaaatggaaatttgtttatattgactacagattgcca
tattattagtaaatgctgagcacttaatctcgaataaagaactagtttaaaaatgattctaacaatggcatt
gactgttctaccttattactcatgggtgggttcagccaatgtttctgttggagacaaaacaaaaacagtc
aaattaaacaagcagtcacaaacccaacatacagactactgataagaaggtcatatcataagatatggcattga
atltgtgtctgctaattgtaaaaatctgatgccacacagcaaaacttaataaggacctatgtttacattccatgct
caattacattctcctgggttaaacagtcattgcttttaggccctgctgtgtgctggagtttgtctgaagtgtggg
gcttttaagagaaggagaataagcttgctccagagtttaagaaatttaaaactaaaagtcctaaagatgttgga
aaaactattggccttgaagatgtaaaattcattaaagttggagaagacctttatacaaaacaacagaccattc
actgatttgtacccttcaggagacagatgaccggttaattgggtgacaatgggtgaatgttgggttgggtttt
tagaaacatctgcacttggtagctactgtatctaaattgggtgtgacaaaacctgggcacccccatgtgtttggc
catcttgggtcctactcagggccaggtgaaccgagtgccctcttctactgcttcagagtcgaagcagattgt
agtagcggaccagacacagaatataccaccaagcacgttggcgcaaaagcatactgggaagggaggcttctgt
gaacatgggtgctggttctcaaacctcagtgctcaaaagagtcctcctgaggattcctggatcacactcttaa
cttctcattcagtaggtgttagctgggtgagatctgcatttttttttttttctgagaccagtcctcact
ctgatgcccaggtgagtgattggcgccatcttggctcactgcaacctctgctcccaggttcaagcaat
tttctgctcagcctctctagtagctgggattacaagcacatgccaccatgcctggctaatttttgtactt
ttagtagagagggggtttcgccgtgttggccaggtcgtcttgaactcctgacctcaggtgatcccccact
ttggcttcccaagtggtgagattacaggtgtgagccaccatgccagcctgaatctgcatatttaacaagc
accacaggtgattctgatacagtagctccccaaacctcacagtggttagtgaatcccagtcatttacaattct
gccatgattttgggtcatattcaagtgacagctggtagcatttttagttaatatatttttaaatlaagtcact
tcttttggataaattaaatttaattacaagggaaagctataccactgctgtaaaaacatcacctgctttaaaga
gaaggtacataatgaatatacattaaagataaagatgtatatgtgtgtgtgtgtgcacataaagtatacaca
tacctaccatagggatgagtttctccttcaggttttccaaactgaaatgtcaactttgaggccagtttaatatg
tgtaagatatatgtgtgtatgtatgtctatacatatagacataacgtaaaaacatacatggatgcataatag
tatatctatacacaacctattatgcataatcatgtatatttcatccacttagtattatcttztattttgccc
tttggcaaatgctcagtaaaagaaaaggggttagaaggggagaaaggcattttatcccaagccttcaggaatc
aggatgaggatgtcttcacctgtgtgggtggggagtagattatacaattagagacagcacattggagztgtggc
tgatatgctgtgtgatgtagctctagctctcgcctagcagaggaaggacatttcaatagaagaaaaagtt
taagaccttgccgagaaacagagaaaggatgtttgtcttttaagaagttgaaaacctgtttgcagacaaa
agccctccagttttggcagtaaaactttcatgcaaggggaagaaaaaggcaggggatgacattgttgacaattg
tgaggaattaccatgtgccaggcactgtgagggggctttgtacatatcctctagtttttagtgcttataaaa
actctgtgatattgtgcacagcatttttaaaactttgctgcatagtcgagaaaaatggaaggatggggaaatttgag
tcatttggccagggttctatagctaccccaggttcccatgactggagaattggggcacaggggtggcggggga
gagtgagtgacaagaatcctaacaatcttatttccattgagtccttataaaagaagtggaattaaactaccacg
tttttaagtttttcttaaaatttaggttatgtggatctggcggttcttgttttgcctgggtttgttttgtt
ttgctatgctgtcttgaacatctgtcatctttaggcctaacggtaaacacaaaaaacacttaccctcctata
gctttcaattagatctctcagtttgtgtttgttaattagttttccaggcaagttctcctaggttcggcttct
agtggtttaaccttttagttataaagtgaacccaaagagagaaagtagaaacaaaacacctcacctgttttgg
ctcatgaattactctctatggaaggaacaatcatgaacacctctgctatcacagaggcctatctgagtcgtg
acgtttaaggggagaccgctgaggtccctttgaggactgtgaatgtgggagtcctgggactctgggtgaagaac
ccgttccagaagagatgaatgagctgggacaggttcttccatagaacctttaggcaggtttctttagaaatgc
acattgaggatttatgcttgatatttgatgatcagaatgataactcaatccctctgcatttggaaattctct
ttgaaagaaaacatcccaggcagctatttctcagagatagtgagtcacagccacttctagacattttcttgt
gtagtcacattataatttcacagcagtcctctgatatgacaaatgtcaaaatagcccaaccttctctaaact
tcagagatgtctgatattgaataaaacaatgctcatagaaacatcaagaaaggtggattttccctgg

atacttttttctgtcttgacaaataacagtgaaagaaactgatctcacgtctttttctctttggaagcctgaa
cactcagaacccaacttgaggctcctcagctatagcaattctgacttcacagctctgtaaattattgttcttt
ttttctcttagcttatgtctttctgcccataatttatcttttccctgttctaataattattgtcctatatctg
ctgtgcagtttaggtgacatataacagcaattaaatatatgaatttggtacatataaagatttgactaaaactc
gatgtaaaaataagtggtctacattcaatttccagtggttagaaacagtggtgacttgaacagagtgacagaa
ttccatctttccctatttttgacagcttttaaactttatattttcttctctttctgtgagccgtcattaactt
tggttctcaaagzccattcccgtattacccatcttgcagacgcagacagatttggaatttgcggtcagagt
tgtattggacacatccccccagcccacatgagatccttttaattctattgcatattactagttttaagtaca
atattcctacttctatttaaaaccattaatcaaagaatgagtttgaaaatgaacaaaatgcaaaccttacagtt
agaaataattgtagtgtcttttagttttgggttaggagtcggtttcttggttggttaaactcaagattgtgaaca
gttttaattcacttggtttatttccaatagagatttcaggtttacatttgaaattcagaaacaaagttttcttt
ctcattacagAGAACACTAAACTCTACATCTCCCTTCCCGAGCAAGGAGCTGGCTGAAGCCACAAAAACATT
GCTGCATAGTCTTGGGACTCTGGCCAGGAGgttaagttgtgtctttccagtagcaggaagcggatcatccac
tgtatcagtattttctcctgagtcctggcaagaggtccttttgagttgaatatcacatgggatgtaatatc
aattttcaaagtataagtgatgtaaacaataatgttttgatttcttatttttagaaatgaagaaacctaaaa
ctcatagatgtctcagagctaatttggttagtggctaaccagctggatatctagtttagaaccttctccatttt
ttctttttggccctaggtaatcatacatttgtaaagaggagaattatctctgccactgcccattgactgctt
ttgtctgaccagcaattttctcatattgcttcttcagtagcaaggccaatcattttaccaacacacatgctt
gctaactaacaggaataacgtggtaaccctaattcagccctttcccttgaaagcatctggcttctgaggttc
aactatgggaatatgggtctcttaattgaacatttaagttgagtttgcttttaggtccacatggtgacaaatt
atcagagtaattctctgctcctaggatcagaggcctgtaggcacttgcaaaagcagttagctctgactcccag
ccagtgacactccacctttctgactcccagccttgtctcaaattaggcttggaagcgaggaactgtctggt
gtccccagcataggaagctgagccagggggcagtgctcacaacaatacagactttaacgtgtaggatatt
ggaaaaataataattttgtggggaaattgtctcagacttggtccacccttatttttagctgcttctctaactccg
ttttcttttttggtgcttgatctaaacctacccttttttggtgcttgcatcatttttcaaatatcaaaa
aacgaaactttatggttttcaacaatgaaagtattgcatgttcattgtggaaaaatgctgaagacttggaatat
acaaaaatgctgagatcaaacactattgatagcttagtgatattcttctcctgtcctgttctactttcttctt
tgaattctgctcacgtgtttctgactgatgaggtctgacttttgggttctctttccagaggagaagcctct
ttcagcttgccatttggtaccctgggttatgaaggctggtaaccttttttactaggtagagaagctggacca
ctggggttcttccagggggagaatgagaaagagaaactgttttgcaagtcctgtagctatttctctaggggccc
tgttagctgacattgacatgccttgcatgtctgcagatccctcgcagccctctgtcccttggttcatttc
tggccttagagaaagcaaacaggggtctgtaacaggggaggtgcctctaaactcaggggttggttacagct
gttttcaacttacatcactggccctgggttttttttttttctggcattaaaaaaaaaaaaatgggaagcaggtg
atgttcccattgtctgatgtggtggaaactctccaagtgaacaataacgtttttcttggcagctgtttcttg
tgccctgcttgctcctggtccaggacaagcaaggaccatctgctcttcaatagaacacctccagatccct
ttgatcaaaagttaactcattgtctgacttgctatttctgtgagataaatgggagaagatcaataaatgcact
tggttgctcagtcagcztgttggaagttgataatttgaccaaaagcacaaccttgaaaggaaaagaaaa
gggagtgaaatgtctctgagaagctgcctagggttcagacagtggtcaccctttccctgtatgctccacatga
caaacctgagtggggtctcatcatgtccattttgcagatgggcaccaaggctcagaaaggttaggcaactttc
cagtcaccaaatgagtttaattgacaaaactgggattcaaaaccagaactgttggtatccaaaagcctgtgttg
ttgcctgcttcgtgaaaaactccagtagcagactggaatagaaaggagaacctccaagaaagaaaaatagca
ctagcagaacctggaaattgggaggaaatgaggacttgaggaataagatgaatgaaagctgacctgagttt
acatctgggtgatgggaaggaggacagggagggcagctcagatgtccaccagcaccgaccagctgcct
ggcattgctaggtgttgaggactcagcagtgaaacacgctaacttctctgcttcttggggcacgtatagggt
gagagacagaaacaaacaggtcagtggtacaatgccacagggaggtatatgcagtgaaagaaaaagcagggta
aggggcatagagcatgagaaggtgcttttttaagggggttgattaggaagctctctctaagggtgacagt
ggacctgaaggagatgatagcatgtctgtggtgaggaaggaaactccgaacaggaagaatggcagatacaa
agacattgatgctagagcatgcctaaggaatgtgtttaaggaccagggaaagtgaagcaagtggtgggggag
gagaggagctcagagcaggaggaggtgagtgccatacagggcctggcaagactttggattcctgctgggtgag
atgagaatccagcggagggcttgaggagggggacatgatgtgatctagagtttagactgtttacactctggt
tggtgggttgagaagagactgggtgggggaaagggaggacaaaggacattgtgctggattgagaaagcag
aagtcagtttctcattcactcaaccgatgatgttcaataaccaccatcatccgtgggctaaaggatgaag
agcctccctccctgagagtcaggaagcactcccagataaagtgtggagtgtgagctgaggtgtaggagaa
agagtaagagtttaccctgaaacgggtgctgggaagagtcataagtttggaataactcaataatttatggt
gcttcttttagaaagatttgctggctttatgtgggaagaaatttktttttttgattggggagtggtgggttg
tggtgaggctgcctgtggaaagagaagtgaagttttgactcactgttatttaaaaatctctaggcctgttc
caataagcaacaaaaggcaaatggcctgggtctctgtccctttctgtctgtatgcctcgtacaggttatg

aaaagaaaaagttgggaaaaagctgtccacctcacctaattgtgttcttgtggagtggtgtagatgccccctc
tctggagaaaaaaatccttgtggcctctgacccacctctggagagcctagttcccttctggaggcagaagg
caaaagcttaggacctagagagtgctggaccacgccactcacaggaaccagcaggctgtgaggttgaaagcta
ggcatatggagctttccaggctgggtgcagggcctcgtggcccttccccctccccctctgtgctctatagctca
gtcttcccaggcggtgtgaacacgcagtgacatttccaggaatacagggatttattaatgatttcttgtgaa
atgtttggaaatacaaagtactctataaatatttccataatagcattggggctgagaactccacaaagtgccg
gaatacatttgcattgtaagacagaacgctgcctgggtcattgatgcctgttgagtgccagtcacagacactg
cctagggtttctgactcacgctgttgggactgttctatgcagggcaccctcttgtgtggcataggatttgtg
cctcaccacacactgttgttagctttgtgtctttagtgatgagtagagggcagtggtccaggccatgggtataag
catctactgccccccagggttaccaaaaccaagccaagttgtgtctcagcgagctccgtgaagcatggagaa
gttgagtactcagagacatgacgtgacttttcaaaggctgtaagctgacgagggacatagctagggttcaga
cttgagtttttcttttcttttcttttcttttcttttcttttcttttcttttcttttcttttcttttctttt
gattgcagtggtgttggctcactgcaacctctgcctcccggttcaagcaattctcctgcctcagcctccc
cagtagctgggattacaggcacctgccaccatgcctggccaacatttttgtattttttagtagagatgggg
tttaccatgttggccaggctggtcttgaactcctgacctcagggtgatccaccgcctcgacctcccaaagt
actgggattacaggtgtgagccactgcaccggccacagactcgagtttttcatcttaagtcttttctattgc
ctgacactttactgagaccaagatagggaacttcacatacagtagcttttctcccaaggcggaagagggctg
ttcaatttctacactagagttcggggagttttagaaatgagtcagttatcgaggatgagagcagttcctgat
aggctcaaccacaatgagatgtagctgttcagagaaagcattcttttatctataaaactggaagataatcccg
gtgaaacgaagcccagccccagggttccactaactccaggctgtgcttctcaaaacttagtgagcatagga
atcacctgggcatcttgtgaagctgtagatttgaattcttgcaggtcggcagaggggtctcagaatccgcatt
tccaacaatgtctccagtaagtgtgatgtgtctgcctccggaccacagattgggtagccagggttctggcaa
gctcatcccaaggctttgagatgacatcagacaaaatattgttctgggacatggcttttgagaggtcaagaaa
ataagatgttttcttcttcttctcattcccccaaccttgcactgccccttttctccccctccccctcccc
tgtccccatccctgacgccagCTGTTCAGCATGAGAAGCTGGAGTGACATGCGACAGGAGGTGATGTTTTCTG
ACCAATGTGAACAGCTCCAGCTCCTCCACCCAAATCTACCAGGCTGTGTCTCGTATTGTCTGCGGGCATCCC
GAGGGAGGGGGGCTGAAGATCAAGTCTCTCAACTGGTATGAGGACAACTACAAAGCCCTCTTTGGAGGC
AATGGCACTGAGGAAGATGCTGAACCTTCTATGACAACTCTACAAgtgagtgatgcatgcagaccccagccc
tgtcccccaacccccatccccctccttagttctggccttggcctgtgtcatctcctcctctgtgtagcagcttag
atgtctacatgcccattttggccaccagactgagcttctccttagaggagagagggcttctcttgaatagctacc
tgtccccagttctctgaatgcagcctggcacatctcaggtgcacagtagtggttatcaatggaatgaatgat
tgacagccaaccttctgggttttctgggggatgtggaagggtggcttccagggtgatcaagaatgagataatg
gcagaaggacaaaatcctgcaagatctcacttatatatggaatatatgtaaggtagaaagtgtcagtttcaca
tgatgaataagttcctgggatcttgatgtacatcgtgtgactatagtttagtaacactgtatagataacttg
aaatttgcataagagatgagatccgaagtgttcacactacacaaaaaggcaactatgaggtgatggatttat
taacagcttgattgtgtgtgatccttttcaaaagtatacatatattaaaacatcacattgtataccttaata
tatacaatttttatttgtcagttgttaactcaaaaaagctagaaaaagcatttttaaaaaaggatgatgtactgg
tcttaataattaccattgagataagctttataataacataaaaaagaaataacagtaaatgataatagcaaac
aacaacaacaaagaactaacatttaagttagaatttcttgtgcaactgtgcattctgtttaagttatctcattt
taccctcatgataaccctgcagggaagattctttaaccccacatttcataggctcagagaggttaagtgcct
tggttagagccacatcagagttaatccacaagagccaggattcaagcccaaatctgcctggatctgtgctct
ctaagataactgttagtggtggcgtgtgtgttctcacactcagacatttgatctgcctttgtttccattc
ttagctgcaaggcagtggttaagaacctgtgtctccatccactccccacacttaagcacttttgtgggc
ccgtgtgcccgtatgcctcgtggcagcagggatccaatgtcacagttttaggcagtggtcctcttctccttga
aaacttgatgcagggggaaccttttctccatttccaaccacaggtgtgtczztttcagacactgagtgzagga
ggttttgtactttattgtaacacaaagaaaccttttcttctctggagtaaaagcactccagacattcgcaagtgt
ccttaagaagccttaaaaggatgggtattgtaggcaactttaattaaatcccatctcctcctccccagctt
gcaagttgacccaaggaagccttcatttccatgacagacttaattgtgagggcatcctcattaaaaaaaaa
aaattctattatcttccagcatatagaagatacttggtatctaaaaatccctgaaaaacttagaatgaatt
tttaaaaatcagggatcctgctggataaaccacccatttgtctgttacaacttttgtatttgggttttgt
taagtgtacataactagtttgtgttaattaaagagaatttttttttttttttttttttttttttttttttt
cggtgcccaggctggagtgagtgagggccatctcggtcactgcaagctccgcctcccggttcacgccatt
ctcctgcctcagcctcctgagtagctggaactgcaggtgcccgccaccatgccagctaatttttttttttt
ttgtattttgagtagagacggggtttcactgtgttagccaggatgggtctcgatctcctgacctcgtgatccg
cctgtctcgccctcccaaagtgtgggttacaggcgtgaaccactgcgcctgttgagaatttttttttttt
ttttttgggagacagagtttgcctcttgttgcgggggttagagtgagtgacacaatctcggtcactgcaa
cctctgcctcctgggttcaagcgattctcctgcctcagcctcatgcgtcaccacgcccagctaatttttgtat

30/86

31/86

32/86

TTTGGCTGTGAGTACTTTGCCCTTTTTGAGGAGCAGGGCATTGGAGTGCAGTGGGACAACCTGTTTGAGAGT
CCTGTGGAGGAAGATGGCTTCAATCTCACCACCTTCGGTCTCCATGATGCTGTTTGACACCTTCCTCTATGGG
GTGATGACCTGGTACATTGAGGCTGTCTTTCCAGgtacactgctttgggcatctgtttggaaaatatgactt
ctagctgatgtcctttcttctgtgctagaatctctgcagtgcatgggcttccctgggaagtgggttgggctat
agatctatagtaaacagatagttccaaggacaggcagctgatgctgaaagtacaattgtcactacttgtacag
cacttgtttcttggaaaactgtgtgccaggcagcatzgcaaaatgtttttatacacattgcttcatttaattct
cacaaggcztactzctgaagtagttactataataaccagcaattttcaaatgagagaactgtgactcaaaga
cgtaagtaaccagctttggtcacacaactgttaaatgttgggtacgtggaggtgaatccacttcgggttacac
tgggtcaataaagcccaggcgcaatcctcccaatgctcaccgaattctgtatttctgtgtcctcagagggggtta
caactaggagaggttctgttttctgtgagtacaggttgttaataattaaatatactagctcctaaggcctgcctg
tgattttaattagcattcaataaaaaattcatgttgaatttttcttttagtacttcttcttaataataatacatc
ttcttgaccaagtccaagaggaacctgcgttggacagttttcatatgagatcaaattctgagagagcaagat
ttaaccctttttgggttcacttctgatcctccctcaaggaggtatacatgaaatatttattactcctgcctg
aacttctttcattgaatatgcaattttgcagcagctgcagattctggatttaaatcttgagtcttaacttactg
gctgagggaccttggataggctccttatccctcagtttctctcatctctaaaaatggggatggcacctgccccg
tgggttgttggaaaggacttacagaggtgcagaatgtacgttgtacatagcaggtttcagcaaatgttagctc
cctctttccccacatccattcaaatctgttcttctccaaaggatgtgtcaaggaggaaatggacctggctg
ggaaacctcagaatactgggatgatgctgagcttggctcacaacctgtgcttggctttcagGCCAGTACGGGA
ATTCCCAGGCTGGTATTTTCTTGACCAAGTCCTACTGGTTTGGCGAGGAAAGTGATGAGAAGAGCCAC
CCTGGTTCCAACCAGAAGAGAATATCAGAAAgtaagtgtgttgacctcctgctcttctttaaactagtgc
tgctgcctctgtcaactgttgggggcaagcgatgtctcctgcctttctaaaagactgtgaaaccactccagg
ggcagagaaatcacatgcagtgctcctttccaaactcctccatgccatttatgtccaatgctgttgactc
tgggagttcacggtctcgatccctgagggacattttcttgtgtcttggcttctagaagagtatcttttac
ttgccccctccaaacacacatttcatggctctcctaacaagctagaagaaagggttaagacaagcgtgatt
gtggaaccatagcctcgctgcctgcctgtgacatgggtgacctgtgtatcagcctgtgtgggctgagaccaag
tggctaccacagagctcagcctatgcttcataatgtaatcattaccagatccctaactcctctcttggctct
taactgcagacagagatgtccacagctcatcaaggctcctgccttctgggttcttgtgcttagagtggctt
cctaataatttaaataggctcctttctgccagctctctctgtgccccatcccttgattgccccgtgtaaaagt
atgatcccccttagtgtagcacgcttgccgtgtgttccataatcatcttctcctacctcctctttacacctag
ctcctgtttcagtcacctagaaatgctcacagtcgctggaatatgtcatgttcttccacacctccatgcctt
tgtaggtactgtttgtctcagaggagaactttctctcctaacttgccctatcttctcaactcctccttctct
ccaagatctagttccggatccctccctgagcatccctccttgggttctcaggtagtgcagtcactctctgcc
ctgaacttccatggcacgtgaaagaaaatctttttatttttaaaacaattacagactcacaagaagtaataca
aattacatgaggggggttcccttaaactttcatccagtttccccaatggttagcagcatgtgttaactgtagaa
tagtatcaaaaccatgaaattgacataggtacaattcacaaaaccttcttcagatttactagctttatgtgc
gctcatttgtgtgtgtgtgtgcgtatttagttctatgcaattttatcatgtgtgaattcatgttaattactag
ctcagtcagagctgcagaaatatctcattgtcacaaagctccttcatgtctacccttaaztggccaczagccz
acctcccttcttctcagttcctgacacctgtcaaccactaatgcgttccctcggtttttacagttttattatt
tctagaatgttacataaatggaaccatacagtaggtatccttttgatactggcttttttttttttttctactc
agcagttatcccttagatctatccaagttgtgtgtgtcaacagttcattcctcttactgctgagtgtgtt
ccctgggaggggtgtatcacagttccatggcattttttagatgtattttttaaacagctttcagcatcctcta
ttttaattgttcatcaagtcctttttcccaatagactctgaatgctcctttatcatcgattcccatcacca
acatcagtagcccaaataggccctaaataaacatttatagcctcctgcctgcctgagaaaccagggtggacat
ggagagaaggcacttctgaaagtccaagcgcagtgcsctgtgtccttacactccactcctcagtgctttctg
tgggttcatttctgtcttctctcctgtcacagTCTGCATGGAGGAGGAACCCACCCACTTGAAGCTGGGCGT
GTCCATTGAGAACCTGGTAAAAGTCTACCGAGATGGGATGAAGGTGGCTGTGATGGCCTGGCACTGAATTT
TTATGAGGGCCAGATCACCTCCTTCTTGGGCCACAATGGAGCGGGGAAGACGACCACCATgtgaagaagaggg
tgtgttccccgcagaatcagccacaggaggggttctgcagtagagttagaattttataccttaggaaaccatg
ctgatccctgggccaagggaaggagcacatgaggagttggcgaatgtgaacatgttatcctaactcagtggt
ctttccacgtgttagtttgcagtagtttcttctcagcctaaaacaagctggggcctcagatgacctttcc
catgtagttcacagaattctgcagtggtcttggaaacctgcagccacgaaaagatagattacatatgttggag
ggagttggttaattcccaggaactctgtctctaagcagatgtgagaagcactgtgagacgcaatcaagctgg
gcagctggcttgattgccttccctgcgacctcaaggaccttacagtggttagtatcaggaggggtcaggggc
tgtaaaagcaccagcgttagcctcagtggttccagcagcattcctcaaccatttcaaccattccaaagggtta
tatctttgggggggtgacattcttttctgttttcttttaattcttttttaaaacatagaattaatatatta
tgagcttttcagaagatttttaaaaggcagtcagaaatcctactacctaacaacaaaaattgtttttatcttt
gaataatatgttcttgtttgtccattttccatgcagtgcatgttaggcatacaaaatacattttttaagaa

tactttcattgcaaattggaaacttcgtttaaaaaatgctcataactaaaattggcatttctaaccatagggc
ccactttagtatttaccgaagcaaaaggacagcttctgttgggtctggtaggggtcattagaaag
gaatggggggcggtgggaggggttggtgttctgtctctgcagactgaatggagcatctagagttaagggtg
ggtaacacctgacttctgtacttctaatttttgcctcagGTCAATCCTGACCGGGTTGTTCCCCCGACC
TCGGGCACCGCTACATCCTGGGAAAAGACATTGCTCTGAGATGAGCACCATCCGGCAGAACCTGGGGGTG
TGTCCCCAGCATAACGTGCTGTTTGACATgtgagtagcagcagcagcgttaagaataggccttttctggatgt
gtgtgtgtcatgccatcatgggaggagtgaggacttaagcattttactttgtctgtgtttttgtttttctttt
tttcttttttttttttttgagatggagctctcgctctgtgagccaggctggagctgtagtggcgcgatctcggt
cactgcaaccttggcctcccagggtcaagcgattctcctgctcagcctcccgagtagctgggactctagggc
acacaccaccatgcccagctaatttttgtgttttttagtagagacggggtttcaccatgttggccaggatggg
ctcaatgtcttgacctcgtgatccgcccacctcggtctcccaaagtgtggaacacaggcatgagccactg
tgtctggccacattttactttctttgaatatggcaggctcacctccgtgaacaccttgagacctagttgtt
tttgatttttaggagaagtgagggtgaatgggttgagctgtagaggtgacatcagccagccagtggtgggg
gcttgggaaacattgtctccattattgtcatgctggagggcccttagcccatcctctcccccgccaccc
tccttatttagggcctggagcagacttcccagacctggtagtgcctcagggccctggtagtgagacctatat
ttgctgcttaagacatttgcctccactcaggttgtcccatcagccataaggccccagggagcccggtgtgat
ggagcagagagagacctgagctctgcaatcttgggcaaggcttttcccttatgtttcttcttctaaagt
aacagctggggctcatgtgctccctcctcatctaaagtgaacacatggggctcatgtgcagggtcctccccg
ctttcagagcctgaggtccccctgaggtcaggaaggctgctccaggtgagtgccgagctgacttcttgggtgg
acgtgctgtggggacagcccatataagaccacatcttggggccctgaaattgaaagtgttaactgcctgggt
catgggtggccaggcctgctggaaacaggttggaaagcagctgtcacctttcactttgatttctgagcagct
catgtggttgcctcatgtgttctaccttgaatcttgaagattatttttcagaaattgataaagtattttta
aaaagcacggggagagaaaaatatgccattctcatctgttctggggccaggggacactgtattctgggggtat
ccagtagggggccagagctgacctgcctccctgtccccagGCTGACTGTGGAAGAACACATCTGGTTCTATGC
CCGCTTGAAGGGCTCTCTGAGAAGCAGCTGAAGGCGGAGATGGAGCAGATGGCCCTGGATGTTGGTTTGCC
ATCAAGCAAGCTGAAAAGCAAAACAAGCCAGCTGTCAAGgtgcggccagagctaccttccctatccccctcc
cctcctcctccggctacacacatgcggagggaataatcagcactgccccagggtcccaggctgggtgcgggtgg
taacagaaacttgtccctggctgtgccccctaggctcctctgccttccactcactgtctggggctgggtccctggag
tttgccttgcctgtttttttttaggtgagGGAATGCAGAGAAAGCTATCTGTGGCCTTGGCCTTGTGCGGGGA
TCTAAGGTTGTCTATTCTGGATGAACCCACAGCTGGTGTGGACCCTTACTCCCGCAGGGGAATATGGGAGCTG
CTGTGAAAATACCGACAAGgtgcctgatgtgtattttattctgagtaaatggactgagagagagcggggggct
tttgagaagtgtggctgtatctcatggctaggcttctgtgaagccatgggatactcttctgttakcacagaa
gagataaagggtcattgagactgagattcctgagaggagatgctgtgtctttattcatctttttgtccccaac
atgggtgcactaaatttatggtagttgaaagggtggatgcttaaatgaatggaagcggagaggggcaggaag
acgattgggctctctggtagagatctgtgtggtacagtagtaggagcagcaggcaggcttggagccaaactc
tggcztgccctgagacattgggaaagtcaaaactgcctcaccttcttggcgataataatagtggtgcz
tacctcatagaggattaaattaaatgagaatgcacacaaaccacctagcacaatgcctggcatatagcaagt
tcccaataaaatgcztactgttcttacctctgtgaggatgtggtacctatataataaaagctttgccattc
taggggtcatagccatacagggtgaaagggtggcttccagggtctcttccagtgcttacccttgctaatatctc
tctagctccctgtcactgtgacaaatcagaactgagaggcctcacctgtccacacatcctgtgtttgtgcctg
gcagGCCGCACCATTATTCTCTCTACACACCACATGGATGAAGCGGACGTCCTGGGGGACAGGATTGCCATC
ATCTCCCATGGGAAGCTGTGCTGTGTGGGCTCCTCCCTGTTTCTGAAGAACCAGCTGGGAACAGGCTACTAC
CTGACCTTGGTCAAGAAAGATGTGGAATCCTCCCTCAGGTTCTGCGAAGACAGTAGTACACTGTGTCTATC
CTGAAAAAGgtgagctgcagctcttgggtgctgggtctgggtctgggagcagcaggacttgcctggctgtg
aatgatttctccatctccacccttttggcatgttgaaaccaccatctccctgctctgttgccctttgaaa
tcatatcatacttaaggcatggaaagctaaggggccctctgctcccatgtgctagttctgttgaaatcccg
tttcttttctctatgaggcagagagtagtggaaggtccttagaggacattattatgtcaagaaaaga
gacttgtcaagaggttaagagccttggctazcaaatgacactgggtzgttctgctcattacttttcaatctcat
tgaccttaacttttaactataaaacagccaatatatttaggcactgatttcatgccagagacactctggg
caztgaaagaaagtaataatagtttaattttatatagcgttggtaccatttacaacctttttttttttt
taacctctatcatctcaattaaagtgcagagagaccctgggaagaaggttaactatatttattatccagatg
agggaagtgaggctttaggggaattggtagctgattcaagggtcaccagcaggtaataaacagtgggtgggac
cagacccaattaccaggtatgttttctctgtaccgcagtagatgcctgagatttatttgggtgttgtagcc
agtggtagcctaattgtattttacatcccaacctgaaactcctatccacttatttaccttttaatgagcctctta
actcaagtgcagctctgaggaccagcagcatcaggatcacttgggaacttgttagaaattcagcaacctgggg
ccagctcagacctaccgaatcagaatctgtgcattttaacaagggtcttgagtgggtgaacacacattaaag
catgagaagcattgaactagacatgtagccaggtaaaaggccttgctgagatgggtggcaaggcctcattg

cagcattcattggcaggccacagttcttttggcagctctgcttccctgacctttcacccctcaggaagcgaggc
tggtcacacggccacacacatgccagacagggctcctctgaaagccacggctgccagtgcatgtgtcccaggga
agctttttcccttttagttctcacacaacagagcttcttggaaagccctcccggcgaaggtgctgggtggctctg
ccttgctccgtccctgaccctgtctcacctccttcttggccatcagGAGGACAGTGTCTCTCAGAGCAGTTC
TGATGCTGGCCTGGGCAGCGACCATGAGAGTGACACGCTGACCATCGgtaaaggactctggggtttcttattc
aggtgggtgctgagcttccccagctgggcagagtgaggcagaggaggagaggtgcagaggtgggtggcg
tgactcaaggtttgctgctgggctggggtgggtgctgctgggkggtgggagcagcttgggtggcgggtggcc
taatgcttgctggggtgctggggtcggtttgggagctagcagggcagtgctcccagagagctgagatgatt
ggggtttggggaatcccttaggggagtggaactgaataccagggatgaggagctgagggccaagccaggag
gggtgggatttgagcttagtacataaagaagagtgagagcccaggagatgaggaacagccttccagattttct
tggttagcgtgtgtaggaggccagtgctcaccagtagcatatgtggaacagaagcttgacccttgctatctc
tgctagtcccaatggctggcttttccaggaaggtcttctgcttccatggactgttagattaaccctttatt
taggtaaatgaggaacactactttataagcataggaaaggggtgaagaatcttttaagattcctttactcaag
ttttcttttgaagaatcccagagcttaggcaatagacaccagactttgagcctcagttatccattcacccat
ccaccaccacccacccatccttccatcctccatcctccatcctccatcctccatcctccatcctccatcctccac
ccattctacactgagtagcttataatgtgctggctttgggtgatacaaaaggtgaataagacatagtcctttcc
tttgccccaacccctcagaccagagatgaacatgtggaatgacctaaacacctggaacaggtgtgggtgatg
agcggcaggcctctgatgagaggggtggggatggccagccctcactccgaagccctctcagttgattgagc
catctttgcatctcggctccctgcagATGTCTCTGCTATCTCCAACCTCATCAGGAAGCATGTGTCTGAAGCC
CGGCTGGTGGGAAGACATAGGGCATGAGCTGACCTATGTGCTGCCATATGAAGCTGCTAAGGAGGGAGCCTTT
GTGGAACCTTTTATGAGATTGATGACCGCTCTCAGACCTGGGCATTTCTAGTTATGGCATCTCAGAGACG
ACCCTGGAAGAAgtaagtttaagtggtgactgtcggaatatatagcaaggccaaatgtcctaaggccagacc
agtagcctgcattgggagcaggattatcatggagttagtcattgagtttttaggtcatcgacatctgattaa
tggtggccccagtgagccatttaagatggtagtgaggatagcaggaaagaagtggttttctctgtaccaca
gtacatgctgagatttggtgtgttgaaaccagtggtacctaacacatttacatcccaaccttaaacctcat
gcacttatttaccctttaatgagcctcttactttaagtacagtgkgaggaacagcggcatcaggatcacttg
ggaacttgtagaaattcagcaacttgggcccagctcagacctaactgaatcagaatcaggagcaattctctg
gtgtgactgtgtcacagccaggtatcaactggattctcatataggaatgacaaacgtttatggatggat
agtctacttggtccaggtgctgagatttggtttttgttttttgatttttttttaactcactgtgacctcatt
aattctcaaaaaagatgaaaaaatgaacactcaggaatgctgacatgagattcagaatcaggggtttgggg
cttcaagtcctcctctcttattccatgtaatgcctcccttagagatacaacatcacagacctgaaggc
tgaaggggatataaaagctgtctggccaagtgggtctccaagcttgacagtgccagcagaatcacctggggata
ttattaaaaataaacataactaaggtttggcttcagggcctgtgaatcagaatttctggaggtgagggctga
agtctgtatttctattgcatactttggacacagtggtctatagactagagtttggaattgattgcgctcatt
cagattctctcttgatgtttgaattgctgcatatattctagtgtctatttctcctgctcattctgtc
ttggataacttatcatagtagtactagcctactcaaagatttagagccacagtcctgaaagaagccacttgactc
attccctgtaggttcagaataaatttctctgcgcagtgctgtcatagcttttttaaaatttttttttatt
tttgatgagactggagttttgtctcttattgcccagctggagtgagtggtgagattttggctcactgcaac
ctccacctcccaggttcaagcgattctcctgcctcagcctccaagtagctgagattacaagcatgtgtac
cacgcccagctaattttgtatttttagtagagatgggttttatccatgttggtcaggctgggtctcgagctcc
agacctcaggtgatctgcccgcctcggcctcccaaagtgctgggattataggcctgagccacagcgctcagc
cataactttaatttgaaaaatgattgtctagcttgatagctctcaccactgaggaaatgttctctggcaaaaa
cggtctctctcccaggttaactctgagaaaagtggttataagaaaatgtggcttctactttctctgtcttacggg
gctaactgcccactcagtaataataaatcgtggcagtggtgactactctcgtaatgttggtgcttataatg
ttctcatctctctcattttccagATATTCTCAAGGTGGCCGAAGAGAGTGGGGTGGATGCTGAGACCTCAG
gtaactgccttgaggagaaatggcacacttaagatagtgcttctgctggctttctcagtgccagagatattg
ttcctttcccttgaaattgttctattgcattctcatttctagagtgtaggtttgttgagatgggggaaggtt
tgttttgttgtaaaaaataaaagtatgggattcttctctgtgccttcagATGGTACCTTGCCAGCAAGAC
GAAACAGGGCGGGCCTTCGGGGACAAGCAGAGCTGTCTTCGCCCGTTCAGTGAAGATGATGCTGCTGATCCAA
ATGATTCTGACATAGACCCAGgtctgttagggcaagatcaaacagtgctcctactggttgaaatgtgaaattct
ctctcatgctctcacctgttttcttggatggccttttagccaaggtgatagatccctacagagtcocaaagag
aagtgaggaaatggtaaaagccacttggttcttggcagcatcgtgcatgtgatcaaacctgaaagagcctatc
catatcacttctctttaaagacataaagatgggtgcctcaatcctctgaacccatgtatttattatctttctg
cggggtcctagtttcttgtatacattaggtgtttaattgttgaaacaaatattcattcgagtagatgagtgat
tttgaaagagtcagaaaggggaatttgctgttagagtttaattgtaccctaagacttagatatttgaggctgg
gcatggtggctcatgccagtaatcccagcgctttgagaggctgaggtgggtagatcacctgaggtcaggagt
ttgagaccagctctgaccaacaaggtgaaaccccgctctactaaatacaaaaaattagccagtggtgggtggc

acatgacctgtcatccagctacttgggaggctgaggcaggagagaatcgcttgaacccaggaggcagaggttgc
agtcagccacggttgcgcatttgcactccagactgggcaacaagagtgaacactccatctcaaaaaagaaaa
aaaaagaattagatatatttggatgagtggtcttctgtgtgttactgagatggagaggagagctaagacat
caaacaaatattgttaagatgtaaaagcacatcagttaggtatcattagtttaggacaaggatttctagaaa
atttttaggaacagaaaactttccagttctctcaccctgctcaaaagagtgtatggctcttacattatata
aactgacctgacttcatacagtatcagtaacttagatcatttgaaatgtgtccacgttttaccaaaaatataata
gggtgagaagctgagatgctaattgccattgtgtattctcaaatatgtcaagctacgtacatggcctgtttc
atagagttagtctataagaaattgatgacttgattcatccgaatggctggctgtaacacctgggttacgcatga
acacctcttttccagttgtctcaagacacctttctttctgtacttatcagacaaggactgaaaggcagagac
tgctactgttagacattttgagtcagcttttcccttggacatagctttgtcatgaaagcctttacttctga
gaaacttctagcttcagacacatgccttcaagatagttgttgaagacaccagaagaaggagcatggcaatgc
cgaaaacacctaagataaataggtgaccttcagtggttggcttcttgcagAATCCAGAGAGACAGACTTGCTCA
GTGGGATGGATGGCAAAGGGTCCTACCAGGTGAAAGGCTGGAAACTTACACAGCAACAGTTTGTGGCCCTTT
TGTGGAAGAGACTGCTAATTGCCAGACGGAGTCGGAAGGATTTTTTGTCTCAGtgagacgtgctgttttcg
ccagagactctggcttcatgggtgggctgcaggctctgtgaccagtgaaggcaggatagcatcctggctcaag
atatggatgcccggagccagatttatctgtatttcaatcccagttctattccttggcagttgtgtatccgctg
gcaagttacttctctatgcctcaatctcctcatctgtaaaatggggataataatattacctgcaatacaggg
ttgttacgaaaaataaaaaatgaataggtgcttagaatggggcctgcattagtaagtgttagttttgtgtgt
gtatatgttatttttatttggaggagaacataaaaaaggacaaagtgtagaaaaactgggtgggtgtattca
ctgtctataacatgagagttgttatgcccagatgcacttgacatgtgaatttattagaaacatgatttttct
ctgagttgtatgtttaactcaaatgatagaaaagataggtcagaatatagttggccaacagagaagacttgt
tagactattgtctgcatgtcagtggttgcagtgtaacttgcttagttagaaaaggttaaatttttctactcta
taaaatcaagaaatatagagaaaaggtctgcagagagcttctcatttgatgatgtggatattgttaagagcg
ggagtttggagcagacagagctcaagttgaatcctgactttgtacttattggctatatgaccttgggcaag
ctgcttagtctctctgatcctcagttaccttggttgtgtgatgaccattgataacacaccataaataa
tgacaacatagagatagttctcattatagtagttgttatacagaattattcactcaatgttaattttctgca
ttgaaatcccagaacattagaattgggggcattatttgaatctttaagggtataaggaatacatttctcagc
aataaatggaaggagtttgggttaacttataaagtatacccaagtcatttttttccagagaagatatgg
agaaagctctaggaggttgaaagaaggaaattggatatttattcttctgagactatcatgggagataatgact
atgggtgtccatgattggagccgttggctgtagagttgggttttattatagtgtaggatttgaatgggcatgt
gttctcagacctcagattaaaaawgagaaaactgagccagtggggagcgtgacttcacatgggtacacttgt
gctagagacagaaccaggattcaggacttctggctcctgggtcctgggttcatggcccaatgtagtctttctc
agtcttcaggaggagggaaggccaggaaccagtggtctgagtcaccctgaatgtgagcactatttactctgtg
aacttcttggcttagtgctctgcccaggtggccataacctctggccttgtgttgccagagaaaaggttagt
tttcaggctccattgcttcccagctgccaagaatgccttgggtgcagcacagtcattagggcctgcattctca
ttgcccgtgctgggttgggtcggggaggtgggctggactcgtagggatttggcccttggccttgtttctaacact
tgccgttttctgtgtctcccttgcctcctcactgctgggttaaagATTGTCTTGCCAGCTGTGTTTGTCTG
CATTGCCCTTGCTGCTTCCAGCTGATCGTGCCACCCTTTGGCAAGTACCCAGCCTGGAACCTTCAGCCCTGGAT
GTACAACGAACAGTACACATTTGTCTCAGgtatgtttgtctctacatcccaggagggggaagattcgagcag
accaaagatgtttacgagggccaagggaatggacttcagaattacacggtggaatgaattttactgctgcgg
ctcaggtccctgtataagctaatactgcagtcataagaacagcagcgaactaacctgaataataggccagtc
ttctgttgagcctttcagcctctctcctcttctactctactgtgtgtcaggaacagccacatgtgttttaggtg
aaataatccaccttgcacaaaatccatgattaagttataaaatatttggatttgggagctgtgttttaatt
ctgtaactgagtcacagggcacactgtcaaagcatagaacctccagagactgttttctgcaaaagtataatt
catgtaattattatctattctgttatatttgggagtttaggtagtggtttgttctttagataaaaaatatcccc
cactctgtaacaatacattaaatcaaagaaaaggacaaaaggattttctgggtcttggtagcaggagctttc
ttcagtcctgaaagatttggtagacctgtagatgggggaactgtgtcagtgatataaaaagggaagcattttaa
aaaaaaaaaagtatatatatatatatatatatatatgtaatgtgaattggcctcttttctcctaagzccca
catttttcttctacatagttcaggtttactttatttttcttctccggctgctgacctgtattgcccgtg
gttgtggaacatagcatgtgtttgtgacctgtgctgttattttgtgtcttctagttgtgcatgcacaaagag
tacaaagttttcttgcctttcttggaaaatcctgctgtctgtgcccaggaagataattgtgaaagcattt
tgaaatacttaattgagttgattttcttcaaattaaaaaaatatataaatgtatatgtgtatgtacatgtgt
gtacacatacacacctttatacatagcccatttaaaacaagctccactttggagtgctctacgtcacct
gatgccgaatacagggccagagctgtgagatccttctgggtgggtttctgtgtttgttcttctgttttaag
agcctgtcacagagaaatgcttctaaaatgttttaattataaaaacattttatctctcagattactgtgtt
taattgaattactaagctggctgctctcatgtaccacacagCAATGATGCTCCTGAGGACACGGGAACCTGG
AACTCTTAACGCCCTCACAAAGACCTGGCTTCGGGACCCGCTGTATGGAAGGAAACCAATCCCgtgag

tgccacttttagccataagcagggcttcttgtgcttggctgggttgatttctaataatgctgcatttatca
actgcatgccacattgtgaccgccagcatttggcccttgaattattattatggtttatttacaaaaagcgaa
ggtagtaaccgaactaaattatctaggaacaaacgcttggagagctcttctaacaccgtgcaaagcacgtcat
tacagacatttgtttactgatttagaaccttaatatatttaatttaaatazgcactttacacttactgatgaaa
tgcttttcttcttctctctccagccctgtacttaagtgtctcaataggctctcattatatatgattttt
aggttttgcttcatcagcttcttctgcttttataatctgaaaagatggcataatgaatttttataaaaaaggga
ctttcttcttctcaaatgtatatatttttattgtacttctcttcaaaaccccttttaaaaagtaagcagtgg
ataaataaattcagtgagcatccatattgacccttaagttagtgtaggggaagggaggtcaccagatcactg
tgagtgaagatggtagagaggtgaggatcttatgaggccgtgctcaaggctggtagaggtgggttagtggtt
ccaggttttaggcagaatctcagctgaggtcatgaaacaacagtgatctctgaaaaattatggcaagtgagatg
agggtctggagaattggagagggggcacaacttgactttcaagtttcaatgggaagatagggtgactctgcaca
ccacagaacagtgagcatgataacctgtttatacaaggttctagagcagatttctaaatggatagctactgt
gtgcttgggttgttcttaattagttatggatagttactaaatacttgttagtacttagtacataatgggtgggt
aaactctagcagctaatttgggttcccaataaccagatgacaaggatagagaaggacacagacacggccta
tctggatttctaggtggcttggattttccacatgaaggttggtaggggaagatagaagcatgagagtgagatg
ataatatagttatctggattcatcactggccagctgaaccatattgaactcatggattgatgctagcttagga
aggctctgtaggagccagaactgggctgagagccagcccatagagacaaaagagggcccgccctgacatcag
aggggtcaaacatgatgtctgagcccccactacagctctgcccggaggtgggtggaaggaagagcctttatcct
tacaatttctactgaaattcaaatttttaggttttgcaaaaaaatggtaggacctgaaggaaatttgacagga
gcattgtctcagctgtattttaaatttgtctcagccaatccccctttgaatgttcagagtgtgaagcttcaggag
ggcagcgctcttagtgtagcttttctggctcagttcaggtgctttaaggagacaattagagatcaatctgga
aaacttcatattgaatttttaatacatagaacaaacaaataagaaatagttaaaaatatatatatatataata
tatgt
gagatggagctctcgctctgttggccaggtggagtgagtggtcgaatcttggtcactgcccactctgcct
cccaggttcaagtgattctctacctcagcctctctgagtagctgggattacaagcatgtgccaccacactgg
ctaatttttctaatttttagtagagatggagtttcacatgttggaacaggatgggtcttgaaactcctgacttag
tgatccacccgcttctgcctcccaagtttctgggattacaggcatgagccatcgtgcctggcaattatattt
aatatttaataaaggaataatttgcgtgaactttacttttaatttgggaattctgaaactggaagggaac
tggaatgacttgttgaatcaaatcattttaacttttattttgcccagtggaaaaaataagcccccaaaaga
gcaggggacctgctgzatgtcccacagtaattcagagctggagatgaggttgaaggctttgtgtcttatctc
cagggaaaattttagacagcgtagctctztatgtgacgagcattctcaccacagtcaccccccaattctc
tactcatttgagaacataaattggatcttggcagctctctactcatttttcagcacatcgagcataagattca
gactctttccagggcctctctcactctggctcctctcctctctctctctctctctctctctctctctctct
ctactccagccatgctgtcttctctattatttcttaaaaaartagaaatgcatttcttctctagggcctttgtacc
tgcacttggcatcgcttttgcctcagaatgttcttttggccaagcttttggccagcttgttctccatcattgt
tatgttttggctgaaatgtcttctcttagtaggttcattctccccagtcactgtcttttatttttgccttat
tttggggccattcaaggttatcttatttagtgatttttgggttctctctctccatgggcatacacctcagtgaa
ggcaggtattttcaccttagggcctcgaatatactggacagcatctggcacgtagtagatgctcaacgaatg
tttgttgtgtgagcaaatgggttggttgattggattgaactgagttcagtatgtaaatatttagggcctcttt
gcattctattttactttatgtataaaatgatataaatgatgatataaatgatgtcacagtgtacaaggctgt
tgtgggatcaagcaatcaaatgagatcatgcttgccttttccaaatgggtgagggaaatagatgcatgtttgtg
gttgttacggaatgatcctgtgctcctgagggaacagaaaggccagggccatctctggtaatcctactcttgc
tgtcttccctttgagAGACACGCCCTGCCAGGCAGGGGAGGAAGAGTGGACCCTGCCCTGCCAGTGTAGCAGCG
CCATCATGGACCTCTTCCAGAATGGGAACCTGGACAATGCAGAACCTTCACCTGCATGCCAGTGTAGCAGCG
ACAAAATCAAGAAGATGCTGCCTGTGTGTCCTCCAGGGGAGGGGGGCTGCCTCCTCCACAAGtgagtcact
ttcaggggggtgattgggcagaaggggtgcaggatgggctggtagcttccgcttggaaagcagaatgagtgag
atatcatgttggggaggtctgtttcagtccttttttgttttttgttttttctgaggcggagtcctgtctct
ggctgcccaggtggagtgctgtggcatgatcttgcctcactgcaacctccacctcccaggttcaagcgatt
ctcctgcctcagcctcctgagtagctgggattacaggcacgcaccacatgtctggctaatttttgtgtttt
tagtagagataggggttctgcctgttggctaggttggcttggaaattcctgacctcaggtgatccaccgctct
cggcctcccaagtgctgggattacaggcgtgagccactacgcccagcctgtttcagtcctttaactcgtct
cttgtcataagaaaaagcatgtgagttttagggggagaaggtttggaccacactgtgcccattgctgtccca
cagcagtaagtcacaggacagactgtggcaggcctggcttccaatcttggctctgcaacaaatgagctgggt
agcctttgacaggcctgggctgttcttccactctgaattagggaggtggaccagaaaactcctgtggat
cttgcgaactctggattcttagagactctgtttgggaaggagtcctgagccatttttttcttcttgagaat
ttcaggaaggagtgcttatgatagctctctgctgttttatcagcaaccaaattgcaggatgaggacaag
caattctaaatgagtagcaggaactaaaagaaggcttgggtaccactcttgaaaataatagctagtcagggtg

cggggtggctcacacctgtaatctcagtatcttgggatgccgaggtggactgatcacctaagggtcaggaggt
cgaaccagcttggccaatgtggcgaaacctgtctctactaaaaattcaaaaattagccaggcatgggtggc
acatgccctgtaatcccagttacttgggaggtgaagcaggagaattgcttgaacctgggaggtggaggtcgc
agggagccaaaattgcgcccactgtactccagcctgagcaacacagcaaaactccatatcaaaaaataaaatg
aataaaataacagctaattctagtcacatcagtaatactccagtgaaacagaagatttattagggcatagtgaatga
tgggtgcttccataaaaatctcttgactacaaagaatctcatttcaatgtttattgttttagatgttcagaataa
attcttgggaagaccttggcttgggtgtaagtgaattaccagtgccgagggcaggggtgaaccaagctcag
gtgggttgactgagggcaggtgtctgggacctgtagttaggtttccgggtcacactgtggacatgggtcactgtt
gtccttgatttgttttctgttcaattcttgtctataaaagacctgtatgcttgggtttcatgtgatgacaga
GAAAACAAAACACTGCAGATATCCTTCAGGACCTGACAGGAAGAAACATTTCCGGATTATCTGGTGAAGACGT
ATGTGCAGATCATAGCCAAAAGgtgacttttactaaacttggccctgccktatattactaattagagga
attaagacctacaaataacagactgaaacagtgggggaaatgccagattatggcctgattctgtctatttgg
aagtttaggatattatcccaactagaaaagatgacgagagggactgtgaacattcagttgtcagcttcaag
gctgagggcagcctgggtctagaatgaaaatagaaatggattcaacgtcaaattttggcacttagtagcaactt
gaccaggtaactgggtatccttttaaagccttagtttatctaaattgtgatattaatgttgcctctataagt
ttgtcatgaggactaaataaatgggtgtacatagagtgccttgggtactctctgatggggactccatgata
atttgggtctcatggaggagctctgggaaggttttagggcctgccttgggtctgcagccttgggagagcc
ttctagcttcccaggacatggcagcctagtgtgaatgcttgggtcagcaaatgttgggtctcgtttccttc
ccatcaacttgggtcagttggggctcttccagtttaggagtatctcagtgactttaaattggcatgggcatgctgg
agtgatagttagcatgagtttctaaagaaagacataatttctccatattgtcatccacaattgaaattat
tgtaattgaaaaagcttctaggccaggcaggtgggtcatgcctgtaatcccagcactttaggagggcaag
gcgggtggatcactttaggtcaggagtttagagaccagcctggccaacatggggaaacctgtctctactaaa
aatacaaaaataagctgggctgtgtgtgtgcctgtgaatcccagctacttgggagggctgaggcaggagaat
tgcttgaatctgggagggcggaggttgcagtgagctgagttcatgccattgcattccagcctgggcaacaaga
gcgaaccatctcccaaaaagaaaaaaagaaagaaagcttctagtgttgggtacatcttgggtctataag
gtggttggtaaatgtgtttaaaccgaaggcctgttctcatataagtaattaggtatttatgatggagagaag
gctggaagaggcctgaacacaggtctcttctctagcacaccctacaaggccagctgattctagggttat
ttctgtcgttctcttatctcaggtggatatttactccttttgcacatttaggaatagggtcagtgcttt
cttgaactgatttttgttcttctgtctctgcag**CTAAAGAACAAGATCTGGGTGAATGAGTTTAG**gtaa
gttgcgtgtcttctggcacgtttagctcagggggaggtgggtgtgtagggtgtzcttggattgaagaaagcc
ttggggattgttctgactcacacacttgtgggtgccatctcactgtgaggaggacagaagccctgtgaaca
tgtggagcacacaggggacacagacagatttagattaggcctgctttatagagtttctgcctagagcatcatg
gctcagtgccagcagccctccagaggcctctgaaatatttgatatactgatttcttggaggagaatcaga
aatctcctgcaggtgtctagggtttcaagtaagtgtgtgtgaggggaatacctacttgcatttcccc
caaacagatttcccgaggttcttaaggactcaaggacaatttctaggcatttagcacgggactaaaaaggt
cttagaggaaataagaagcgccaaaaccatctcttgcactgtatttcaaccatttgtccttctgggtttt
gaaggaaacaggtgggactggggacagaagagttcttgaagccagtttgtccatcatggaaaatgagataggt
gatgtggctacgtcagggggcccgaggctccttgttactgatttccgtcttctctctccttccccca
agggccaggaccctggatctctgggcagagcagacgcaggccctataatagccctcatgctagaarggag
ccggagcctgtgtataaggccagcgcagcctactctggacagtgcagggttcccactctcccaactccccat
ctgcttgcctccagacccacatttcacacmcgagccactgggttggaggagcatctgtgagatgaaacaccat
tctttctcaatgtctcagctatctaaactgtgtgtgaatcaggccaggtcctccctgctgggcagaaacca
tgggagtttaagagattgccaacatttattagaggaagctgacgtgtaactcttzzgaggcaaaatttagccc
tcccttgaacaggaatttgactcagtgaaacctgtgacacactgcactgagctgtgctgctgatgatactgtg
caccctactgtctgggttttaattgtcaggtgtgtctttag**GTATGGCGGCTTTCCCTGGGTGTCAGTAAT**
ACTCAAGCACTTCTCCGAGTCAAGAAGTTAATGATGCCATCAAAACAAATGAAGAAACACCTAAAGCTGGCC
AAGgtaaaaatatctatcgtaagatgtatcagaaaaatgggcatgtagctgctgggatataggagtagttggc
aggttaaaccggatcacctggcagctcattgttctgaatatgttggcatacagagccgtcttggcatttagc
gatttgagccagacaaaactgaattacttagttgtacgtttaaaagtgtaggtcaaaaacaaatccagagggc
caggagctgtggctcatgcctgtaatcctagcacttgggagggctgaagcgggtggatcacttgaggtcagg
agttcgagaccagcctggcctacatgacaaaacccgtatctactaaaaatacaaaaaaattagctgggctt
gggtggcacacactgtaatcccagctacttgggagggctgaggcaggagaattgcttgaacctgtaggaaga
ggttgtagtgaaccaagatcgccaggttgcactccagcctgggcaacaagagcaaaactccatctcaaaaaa
caaatataatccagagattttaaagctctcagaggtgggaggggtggcttacacctgttatccagcat
tgggatgccgagggcgggcaaaagcacaaggtcaggagtttgagaccagcctggccaacatagtgaacccctgt
ctctgctaaaaacatagaaaaattagccgggcatgggtggcgtgcgctgtgaatcccagctactcgggaggt
gaggtgagagaatttcttgaacccgggagggcggaggttgacgtgagccagattgcaccactgcactccagc

39/86

acccatctcttgtcttctcctgggtattatctgtccctccctgcttttagagctcctgaaatttgctagaagcat
gtcttcatctaagttggtgataaacacatcaagtaggattggactgaggcagagccctgtagtctgaagctg
cagttcttcttagcggctgacaagccccactatcacttccctgctgggtgctttgctctgcccagctgtgaattc
tcataattgtcctatcgtcaagtcctttatttctgcattttactgcttgatacactgtcaggacagactttaa
aattattctcagtgcgatgaaacaattctgacattcatgttatgagcagttacctcataaatagattacatg
tgagattgaacttgggcagactataatatagcattaatgatgaaacagacacagtcattctcggggaagaaga
atagaggcttatttgctgctgtgaaattaaaattactctgactgggaatccatcggttcagtaagtttactg
agtgtgacaccttgggtgactgttggaagacagaaagggcatgtagtttataaaatcagccaaggggaaa
atgcttgtcaaaatgtattgtcgggtatttttgattaatagtttatgtggcttcattaattcagagttactct
ccaatatgtttatctgcccctttctgtctgataatggtgaaaacttgtgtgatgcattgtatatttgattta
ggggtgaactggatgtctttgttttctacttttagTGCAATTACGTTGTCCCTGCCACACTGGTCATTATCAT
CTTCATCTGCTTCCAGCAGAAGTCCTATGTGTCTCTCCACCAATCTGCCTGTGCTAGCCCTTCTACTTTTGCT
GTATGGGtaagtcacctctgagtgaggagctgcacagtgaggaataaggcatttggtgcccagtgctcagaagga
gggcagggactctcagtagacacttatcttttgtgtctcaacagGTGGTCAATCACACCTCTCATGTACCC
AGCCTCCTTTGTGTTCAAGATCCCCAGCACAGCCTATGTGGTGCTCACCAGCGTGAACCTCTTCATTGGCAT
TAATGGCAGCGTGGCCACCTTTGTGCTGGAGCTGTTACCGACAATgtgagtcagtcagagagaacactcct
gctgggatgagcatctctgggagccagaggacagtggttaattgtgatcttattccactgtcagtggttatt
gacactgctgactgcttctcagagctctgtcttccctgagaaggcaagcaccttcttcttctg
ctgtgcttaccattttgtggtcaagcctttcagtttcttttgacagtttttttacttcttcttcttcttca
atgttgctcttaccagagtagctcctctgcttccactttacacatgagagctgggcgagcgcattcagtc
ctaaggcttttaccatcacctctcttgggtgtttttattgtcatctctaagatcaatgcctttagccttgatc
ataaccttgaactctaattctcaaatctcacttgcctagtggattgctccatttagatagatatagataacc
ccaacctggatatgtcctagttttcttctcccttggaaacttaatgcttttcttgccatccctgtcacactca
gtggcactaccatccactcgggtgcccgaagctgggtctttagagttatcctagatgcttgccttgctgttgca
gatttcccacattcaactgggttatgttgtcagttcttccaggtatggacctctaaaataaggtctcctctc
attccggttgctattgcctttgtccaaacacagcacacaaggccttttacagttgcacaactcttccctgccc
ataccaccacaccccttcccagctgtaagcttcagatgagttgcttcccaaccaccatgctcctgtaggcct
ggcttgaaatgccccttcttctgtcacagggtctggtagtatatcccttgcccttcaagatttagctaaaatg
tgaagctttccttacctgctgggaggtgtctctcttctctgtgctctcagagtccttagtccatgcctc
cagtacaacgtacatccacttacatggtaatttctctgtttacatacttttctactcggagtgaggtctgtt
tcttaataattttgctctctccatgcccctagcagtgcatccagcgtagcccttattcagttggtaga
tatttggccactgttgccctgtgggtacataagttctgatgtatttgagaagaatttctaaaattctgacaa
aatcctgaaactcaaatattgaccagacatgagcaatttgcttttcaaatgctaagggtattttaatggat
ttgctttaattaaatctagcctgtttctaaagctttattcattatttctccatactcagagcatttctccaga
ttttctaaagaatagaattttattgtcatatcatcagctatgcctgctgctattttaattggtagaat
taaaaggtcgtgttctgcccagagaatcaaattttttcttccactcccatatttccagaacttgatacatttt
taggataaaaccatgaatgacacccgtttcttctccctcaccctcccttccctcccattttttttttttttt
tttttagAAGCTGAATAATATCAATGATATCCTGAAGTCCGTGTTCTTGATCTTCCCACATTTTGCCTGGG
ACGAGGGCTCATCGACATGGTGAAAAACCAGGCAATGGCTGATGCCCTGGAAAGGTTTggtgagtgaaagcag
tggtgttaggatgctttaatggagatggcactctgcataggccttggtaccctgaactttggtttggaaaga
agcaggtgactaagcacaggatgttccccacccccatgcccagtgacagggctcatgccaacacagctgggt
tgtggcatgggttttgtgacacaaccatttgtctgtgtctctgatagcattgagaaaagtgaaggggcagtt
ttgaaggtaaagaaaatagtggtattttgctggatccactggctcatgccactgtctgggttggttagaagc
actggaaaagtcaaacataactttgagaattaggtgatcagggaaatcagaaggaaagatgcaaaccttggc
tcttttaggcgaatcatgtgctgcatgaggtcatttatttcttttacacagctctataaaattataatg
tattacatctttttctacctttagaatgggttaaaaatatttctccggtagccatattgattattatcatcca
ttagataatatagtc aaatgggcatgttatttactgttcatagaagaggggctttttgcaacttgggctac
aaaggagatatgtaaggaaatttaaggaaatgggtacatggaactagatttaattgaatctagtgggttaattg
attcactaggatatatgctactgaaaggggaatctgcttaagtgtcttctgatatttatttactaaaaac
ttagaattttattaaaaatactgactgtgaaaattacttgggtcgtttgcctttttaaaggatttttggcat
gtctcattaaaaaaagaaatactagatatcttcagtgaaagttacaaatcgaatacacattggctctgaaatt
ctgattgatactgggtcataaaaagttttcccaaatcagacttggaaagtgatcactctctgttactcttt
tttcttctgtcatgggtgatagccatttgtgtttatttggaaagatcggtgaattttaaggaacataggccaaa
tttgagggaagggccatgggttttgatccctccattctgaccggatctctgcattgtgtctactagGGGAGAA
TCGCTTTGTGTACCATTTATCTTGGGACTTGGTGGGACGAAACCTCTTCGCCATGGCCGTGGAGGGGGTGGT
GTTCTTCTCATTACTGTTCTGATCCAGTACAGATTCTTCATCAGGCCAGgtgagctttttcttagaacc
gtggagcacctgggttgggtcacagaggagcgacagggaaacactcaccaatgggggttgcatgaact

gaactcaaaatgatgtataaaactgattttcctgatgtgggcatcccgcagccccctccctgcccacctcg
agactgtggcaagtaggttttataatactacgttagagactgaatccttgcctgaaaaatagtttgaagg
ttcatttttctgttttttcccccaagACCTGTAATGCAAAGCTATCTCCTCTGAATGATGAAGATGAAGA
TGTGAGGCGGGAAAGACAGAGAATTTCTTGATGGTGGAGGCCAGAATGACATCTTAGAAATCAAGGAGTTGAC
GAAGgtgagagagtacaggttacaatagctcatcttcagttttttcagctttatgtgctgtaacccagcag
tttgcgtgacttgcttaataaaagggtcatgtgtcccaaatgtacatctataccaaggttctgtcaatttta
tttataaaacaccatggagacttcttaaaagaattcttactgagaattcctttgtgatatgaattcccattct
cgaatacattggttttatgcttacatttatgtgttagttattaaaacatactaatttgatatcttagtc
aaaactgaggttagagagaataaatgggttgattttgagtttgagtttcatagtccaaaagctgatataattgc
ctgtgttcaagaggttctatatcagccctctagatgccagcatctccaaattttacttttttggaaatctgta
cagttttgcaatattttattacaaatttctactctgtggaatttaatttttaaaatacctgcaatacata
tatatgttgaatagatgaaaaattatgtagatratatgaatgatacgggttctaaaaagacaggttaaaaag
taagttcactttttattttgagcttcagaatcattcagaagccagtcgccacaaacgcagacaaaggctcttg
gcacatcaaatatgcctatggcttagggttattgacaagcttctatgttgagtgatgtggtttatagtcct
gccttccacagttgcttgggagagctgtgagtcactgaggttatgaatgtttacattttgtttgttgcaA
TATATAGAAGGAAGCGGAAGCCTGCTGTTGACAGGATTTGCGTGGGCATTCTCTCTGGTGAGgtaaagacac
tttgcctatattgcgtttgtccctattagttcagactatctcaccatcaagcaacgatgcgttgaaga
ggtaaaagtggattttaaaggcttctgtattttatgccaggttgagcaattagtcacgagaagagggagac
cctgtatgtccaagagaatgatttccagagaatccaatacaatttaagaaaaagcatggggctgggagcagtg
ttcactcctgtaatcccagcactttgggagggcaggtgggagcactcacgaggtcaggagattgagaccat
cctggccaacatggtgaaaccccatctctactataaatacaaaaaattagctgggcatagtagtgactcctg
tagtcccagctactcgggaggtgagggcaggagaattgcttgaacctaggagggggaggttgcagatttgc
gctgtgcactccagcctgggtgacagagtgagactcatgtcaacaacaaaaacagaaaaagcacgcacatct
aaaacatgctttttgtgatccatttgggatgggtgatgacattcaaatagtttttataaaatagattttctcct
ttctgggttccgtttgtgttctttatgcccttttgcagagtaggtgggtgczaatttggctazgctggctt
tcattactgtttttcaczaczaataacztttggcctcaacttgacaactcaataatatttataaatacagc
cacacttaaaatgggtcccatatgaaatacatattttaaatactatatacagatgtgttataaaccagaataat
ttgattcttctctgatatttgaagattgaaggtttgaggtagttacgtgttaggggcatttatattcatgtt
tttagagtttgcctatacaacttaattctttcctttcagTGCTTTGGGCTCCTGGGAGTTAATGGGGCTGGA
AAATCATCAACTTTCAAGATGTTAACAGGAGATACCACTGTTACCAGAGGAGATGCTTTCTTAAACAAAAAT
AGgtgagaaaaagaagtggttgtattttgctgcaaaagactttgttttttaatttttataaagaataggttgt
tattttgtattacagtggtatttttagagttcataaaaaatgttgaaatatagtaagggttaagaagcacat
aaaatcatccatgatttcaatatctagagataatcacaatttacatttcttctcagtcctcattctctctt
taacagctttattcaggtataatttatacaataataatttgcctgttttttaagagtataatttagtgatt
tttggttaaattgagagttttgcaaccatcaccacaatccagttttagaacttttccatcccccacatctgt
cttatatacacatataaatgtgccatacaattgagatcatactgtatgtagaatttataaattagttttatt
gttaattgagtgatttatgaattttccagtggtttacatttccctaagatgtggaattttacatttgctacat
aaaatccccctatgtacatgtacctataatttatttataaaattccttataaattgttggacacattagtttc
catttttactatgtaaatatgtccctgtatacatcttttattatttctcaggaacaattcctacaaagta
aattggcctctctaaagagcatacaaaattgactgagccaccgttagggcattttctgagactgacaggtca
caaagcaatctgatctttgggaatacagctacattttataggtctcttagataatgttactctaagtaacttt
aaatatgtggggcttctctgggcttttttttttttgagacggagtttcaactcttactgcccaggctggagag
caatggcgcgaccttggctcaactgcaacctccgctccaggttcaagcgattctcctgcctcagcctcctg
agtagctgagattacaggtgcccgcacaatgctgacctaaatttttgtattttcagtagagatggggtt
caccatgttggccagactggtctcgagctcctgacctcaggtgatccacctgcctcagcctcccaaagttct
gggattacaggtcatgagccactgcgcccggcttctctggacttattatgtggagagatagtacaaggcagtg
gctttcagagtttttgaccatgaccgttggggaaatacattttatctcaacctagttatgtacacacag
acatgttagacacatgtataacctaaagtttcataaaagcagtaacctactgttactaattgttagtgactctgc
tatttcttattctacctatactgcgtcattaaaaaagtcgtggtcatgaccactaaatttatttccaaa
ccactaatgaacaatgactcacaatttgaacacactggacaggggtagccaataaaattgaaaagagcaa
ggaaattaatgtattcatgatctcctctcctgtctcttacatttttcagtagcaattgtaaaggaatcctaa
gagaacagacatctgggaatagcaggcctagcgtgcacaactgctttcctaggcttgctcctagtaccaa
gctcctgacgcatatagcagtggaataaaccagcccatagtaagggttgtcacaggagactgggttgtaag
aactgatttgggttggatagctgtgagggcctggcaggtgtccacgtgtgctcaatcctaattctgaaaa
aggctgacctgggggtgctaatttagatacacagagaggaatgaatgctgccagaaggccaaagttcatggca
atggcgtgtgggtgaggtgcagtcagtcgtggaacgtgaacactgaacttctctcacatgtgattctct
acttgactggcttcatagaaccccaaggccaccccccacacataaattgtgtctctaggttctgtgttgc

tcacactcaaaatttctgggccttctcatttgggtgcatgtgaatgggtgcatatgagtgaaagtctaggatggg
gccttagcggttaaagccctggggtagtgactgagattgttggtaaagaatgtgcagtggttggcatgacc
tcagaaattctgaaatgggactgcacctgcagactgaaagtgttcagagagccagggaggtgcaaggactggg
gagggtagaggcaggaacctgacctgccaggaagagctagcatcctgggggcagaaaggctgtgctttcaag
tagcagcagatgtattgggtatcttggtaaatggagaagcactactttacaggaacattagggcagattgtctaa
ccagagtatctctacctgcttaaaatctaagtagtttcttgcctttgcagTATCTTATCAAACATCCATG
AAGTACATCAGAACATGGGCTACTGCCCTCAGTTTGTATGCCATCACAGAGCTGTTGACTGGGAGAGAACACG
TGGAGTTCTTTGCCCTTTTGAGAGGAGTCCCAGAGAAAGTGGCAAGgtactgtgggcacctgaaagcc
agcctgtctcctttggcatcctgacaatatatccttatggcctttccacacgcattgacttcaggctgttt
ttcctcatgaatgcagcagcacaataatgctgggtctttgtatctgctttcagggtggaaacctgtaacggtg
gtggggcagggctgggtgggcagagagggagtgctgctcccaccacacagagtccttctcctgctttggct
cctcaccagttgtcaggttatgattatagaatctagctcctactcagtgaaagaaccttcatatcatgtatgtg
taggcagcatgataaaattcccaagccagacaaagtcaaggtgctttttatcactgtagGTTGGTGAGTG
GGCGATTCCGAAATCGGGCTCGTGAAGTATGGAGAAAAATATGCTGGTAACATAGTGGAGGCAACAAACG
CAAGCTCTCTACAGCCATGGCTTTGATCGGCGGGCTCCTGTGGTGTCTGTGgtgagtataactgtggatgg
aaaactgttgttctggcctgagtggaatacatgactgttcaaaagtccatatatgtccagggtgttgtatga
ttggctgtcttccccagggacagcagagcaaccttggaaaaagcagaggggaagcttctccttggcacaca
ctgggtgtgctgtacatgcctgcagatgctcccaaatagaggcactccaagcacttgttctctagcgtga
ttgaggtggatgtgatttgatcttctctggaaacattcttctaatactcttctgttcttctcctgaa
aatgaagagtgtggacacagcttcaaaatccccaggttagcaactaggtcatagttcctztacacacggata
gatgaaaaacagatcagactgggaagtggcccttgacctttttctctgtagataaagagcattgatgttat
tacgggaagaagcctttgaggttttatgtattccacctgggtctggaatttgtttctgtaaggctaacagt
tgcaataactagggtaactctgagtgagctggaattaaaaaaggaatttcaccccaatcttactatg
acttcaatagaggtttcagacaaaaagtgtttgttatatacttatcagtcataaaaagataattacaacta
aattggccttttcttccctattttatgtggagaaatttaattacataaaaaagtaactcagaatatttgagtt
tctgtcatcaataagacatttataataatgacctgtttacaaatgaatttgaaagttactctaattctttg
attcatcaagaaataactagaatggcaagttaaaaatttaagctgtttcaagatgcttctgcatttaaaaac
aaatttatcttggattttttttccccccagcaataaagacttattttattcttaattacagGATGAACCCACC
ACAGGTCATGGATCCCAAAGCCCGGGTCTTGTGGAATTGTGCCCTAAGTGTGTCAAGGAGGGGAGATCA
GTAGTGCTTACATCTCATAGgtccgtagtaaaagtcttgggttccctcactgtgggatgttttaactttccaag
tagaatatgcgatcattttgtaaaaatttagaaaatacagaaaagcaagagtaaaacaattattactgaaa
ttatatatgcatattcttcaaaaaatgcaagcccagttataaatactgctcttttctcacttaatatattgtaa
acattattccaaagtgcagtgcatattaggtgtcatttctttagctggatagttccattaggtatatactctt
atttaactattccccctttttagacatttggattatttccaactgttccaaattgtaaacaccactacac
tgaacagcatcatccctatatccacatgtacttgaacagaaatacaattccctaggaagctggaatgctgga
agtcatgggtgatgttctcatgggttacagagaatctctctaaaaactaaaaacctcttctgttttaccgagTA
TGAAGAATGTGAAGTCTTTGCACTAGGATGGCAATCATGGTCAATGGAAGGTTTCAGGTGCCTTGGCAGTG
TCCAGCATCTAAAAAATAGgtataaaagataatttcttgggatagtgcttagtgagaaggcttgatattta
ttcttttgtgagtataaaatgggtgcctctaaaaataaagggaaataaaaactgagcaaaacagtatagtgga
agaatgagggctttgaaagtcggaactgcattcaaatctgtctttaccatttactggttctgtgactcttgg
gcaagttacttaactactgtaagagttagtttccctgggaagatctacctcctagctttgtgctatagatgaa
atgaaaaaaatttacctgtgcccagttactggtagagagcgaagcttggagtcacacacaaatgggtttgcat
cctggccctaccattatgagctctgagccatgggcaagtgactaacctccctgggcctcagtttctctgtaa
catctgtcagacttcatgggtccaggtgaggtataaaggagatcatgtatttacagcacatggcatgggtgt
tcacataaaataagttattagtaaatgataactgggtccttctctcagaaacttatttctggcctggcagg
ggccgccccttttcatggcacaagttgggttcccaggggttcagttattcttttaaatagttttctggagatcc
tccatttgggtatttttctgctttcagGTTTGGAGATGGTTATACAATAGTTGTACGAATAGCAGGGTCC
AACC CGGACCTGAAGCCTGTCCAGGATTTCTTTGGACTTGCATTTCTCTGGAAGTGTCTAAAAGAGAAACAC
CGGAACATGCTACAATACCAGCTTCCATCTTCATTATCTTCTCTGGCCAGGATATTACGCATCCTCTCCAG
AGCAAAAAGCGACTCCACATAGAAGACTACTGTGTTCTCAGACAACACTTGACCAAGtaagctttgagtg
caaaacagatttacttctcaggggtgtggattcctgccccgacactcccgccataggtccaagagcagtttg
tatcttgaattgggtgcttgaattctgatctactattcctagctatgcttttactaaacctctctgaacct
gaaaagggagatgatgcctatgtactctataggattattgtgagaatttactgtaataataaccataaaaaac
taccatttagtgagcacctaccatgggcccaggcatttacttgggtgcctaatcctatttaatttagataaaa
aagtacaaaataggtcctgacacttaagaagtactcagtaaatattttcttccctcttccctttaatcaaga
ccgtatgtgccaaagttaattggatgactgagcagttgggtgatgtaggggtggggggcgatatagaaagtca
tttttggccggcggtgggtgctcatgctgtaatcccagcactttgggaggtgaggagcaggcagatcatg

43/86

tagataaatattctgcttaattgattatgaagctgcactgagatttctgaaaatgctctgtagctgagcttat
ttaataaatgttcacttggtataggggaagctacaaaggcagccttcagtgtccttttggtttattcaacca
aaatataaggacacaaatgttagcagttatactgggaaggtgctgggggtggtggcaatggtgagcaggaaggc
gaagtagatatggaaaacagaaatgataactaatatcggtgattccttctcttttctgttrataagtgtgtg
cagacaacatatgagcagtgctgataaatgtaaatgtattkttcatagctcattaagaatcagtttcagaaa
gagatgtctgcttatttkgctrcttgaagaatccctgtcaaacagtccttttsaggaagtacaagaggctgt
ctctatttgtgacctcaggaatggctgtgacagtgctgtgagcagtccttttctgtggcacagatctgaac
tttgtgtgcagaaaaatcttggtctcaagtgaagcaagatgccccctgagcatcagcatcacaaacttcatcc
tcctatcttgaagttcatgttatagtgaactttaatgaaatcatagaacactgtttcttctgtgzaacaatgac
gagggagaggaaaaaactttattgaaaaataaaaaggcaggtaattagatgaaaaatgttacctcatgagg
ttttgttttggctttttgtttttgttttttgagaaacagaatctcgctctgtcgtccaggctggagtgacg
gcatgatcttggctcactgcaacctccgctcccggttcaagcgattctcctcagcttcccaagtagctgg
tactacaggcatgcccaccacacacagctaattttttagttagagatgggggttccactatacgtt
ggccaggctggctcaaaactcctgacctaaaggtgatccttctgcttgggctcccaaagtgtgggattaca
ggcatgagccaccttgctggccctacccatgagccttgactaaaaacattcttctatctgtagaaaaggcca
aaagaacttttccagattcaaaaaacttggcactttgtaattggtaatgtttacattaaagtaaaaaa
aaaaccacttagcttcagtttcaagtgtttactgtttgtgtcacttcattttaatttctcaacacctgc
cctatgaggtaaaaagtaccattttacatatgagtaaatacagctcagtgagataagaaactcgtccaaagg
tacaggttcagtcagtgagcagagggttcttttggttgaagttagggtatcagttaaaattgaccttga
tcacatcagcatcaatatacattaatttaacaaatattttatgaactttactgtatgccagatacttctta
ggtactagggggtacaatgtagaagaaaaatagaattcctgctcaatgaatttatatttcagtggtgaaaga
tgatgtgtggacaaacacacataatgtattttgacagcaatgggtgctaaagaagaaaataagacatggta
tgataaacaatggagagaagtcagagatggcctttctgaggagtacatgctcagaatcgaataaaaagag
caggagcagcctttcaaggtgggtgcaaggatattcccgggaagaaagaaataagtggtgcaaaagcccg
gggaaaaagccttggcaagctgaggtggtaaaagagctatctgtactaatgtctcttactgagttagcaag
gacaagagtgccaggggtggaactggagagatagcagggaaccacatctcacaggatctcgccagcctttt
aagggtatttggattttattgttagtgcaacaaggagccactggagagttttaaacagtagtggtgtgacct
ctgtttcagaaagaacactggctactatgggaagaaaggacagtaggaagactaatagataatgggtggatt
aactaagatggtagcaacagatagggagctatggtaattgttcagtatccactttggagatagatccagcag
acttgctgacagactgcatgtaagggtgagggaaagagagctagcaaggtgacttctagtttgtgacctga
actaggtagatgggttgtgttaaaaaatgcagtggttatctcagctgaagctcaggggcaatgatggaaaa
agataaaatgtgtgcaagttggctgggctggtggtgcacgcctataatcacagcactttgggaggccgagac
gggtggatcacttgaggtcagggcgtttgacagcagcctaacatgggtgaaaccccatctctaataatacaaa
aaaattagctgggcatgggtgcatgcctgtaattcaagctacttgggaggctgagacaagagaatcgctt
gcacctgggaggcggaggtttagtgagctgagatcgacacattgcactccagcctgggcaacaagagcgaa
actccatctaaaaaagttgtgcaagttattggtacgtatatatttaagcctcgggactgaatgagatta
cctagagagaatgaagatagggaaacttcttgagcctgagatcctataacatttagaagagaagctagccag
ggaaattgagagggactggccagtgagagagagtaaaatctgaagagtataatgccatatgttgaagctcag
agaattattgtttcaggaaggcagaagttgtcaattatgtccaacattgctgagaagatgagtaaggaaatgt
aaatgagtaaaaggcaggaatggctattgaatttgttaagacagaggtccttgggtgaccttccaaaggtcat
ttcagcatgacaaggatgcagacctaaactggaatagattttcagggaaagactgagagggaagggaaggga
ctgcaaatatatagcaaatctatattttggcttgaagggaacagaaaacaggacaacagctgggttacaga
acttttatttggattctttccttgtctgttaataatataaggctgcacctgggcatcatcggtcccttctt
ttgattctgctgttttgccttttaactctacagggcatttcttctggcaggagccttgtacacactctgggtg
ttcatgaccaccacggacttgcctttcaaggcagaagcctgtgattcaaaaacttccattccttccaatcg
actattataaaactcattttgtctagtgcacatactcctttaccttaggatcctgggccaactgtcactaaa
gaaaacaaaccatttctcctcctgggggaatgtgcttcttcaagaagggtgcttagagaatagacattcta
ccttgaagacagaaagtactacaacttcagttgccaccctagtcaggttcataggttactcagtaggtt
aagagatgggtgctgagaatgaagtcagagtttgagttacaaagtgccatttgccttctccttgggacttct
gtggcagggtgtggaacaaatcagattggttgcatatctgtttcttctcctgaaaaatacaattcaaatacc
ttcatagctctgtgacagcaacttataaccaacagacaattggtaattttttattttatgtaggcactcccc
atagccagaacttctactgagtcattcatcggttatccaggaataactttccaaatggagtagtgaggcact
tccaaataacagttatgtaattctgttaacagtggtcctcaaatgacatgtgaaggaatgatgtacttctttt
cagactcacagatctcatatgttaattcagtcacaagtaacttagggcttatcacatgccaggcacaggtaa
tatgacaataatgaaaacaaaacccttgcgtcatagaattcggtttctagtggaagagacatacattaa
caaatcatatataagtaaaacattaatatgggtgataacagaaaaagaaagcaggggagaggatagtgct

tagttcaggttgctgtaacaagagtacatagacaggggtggcttamacaacaaacatttctttctcacagat
ctagtggctgggaagcttaagaccaggggtgccagcatgaagaagttctgggtgaaggcttacattctggtttc
ctcacagtgaggggtcttcacgccccttataaatgcactaattctattaccacatgacctcatctaaacta
actcacaaggccaaacctcttatgttgagattaaggcttcaacataggaattttggggggacaaaaacatt
cagttcttagcagatagggggccactgtgggaggggattacaatcttaaatagggttggtcaggggaaggcttca
tgagggcacaagacctgaggagggcatggaaatgatccacgcagatgcatgtctggggaagagcattccaggca
gaggcagtggggaatggacctcaggttaagagcatgttttagcaagttcagagaaaagcctcttaggtcaggtc
tggagcgagagtggaaaatgtaacaggacagatcatgtaaaagactttagtagaccacagtttagaggcttggaca
ataactctgaggatgacatgaaggtattgggaggggtgttgagcagaggagtgatgatctggtttatat
tttagattattctgactgctatgttgaaaataggggttgagagcagaggggaagggcagcacaccaggttaaga
ccacttcccaaaaatccagatgatgatgggcttgaaccaggagagttgctatagggatgtgaagcaatcaaa
ttctagatatttgggacctgtgacagggtacataatgggtgtatgagagaaaaggcagtgtagaatgactct
gaagttctggcctgagcaaaaacagaaaacctggagcttgccaatagctgagataaagtttctggttaaagatc
aagagctcagtttgggacaagaggggtgtgagatttctaataagacattcaggtggaggtgtggggaacacac
ctggatgtgatgagcctggaattcaaatccacatgtgtgaatttgaaaaaagattcagaaaagaggtgtgga
ctggaggagctatccacacacagatagcatttgaagccacaagactgggggtgatgacgcaggggaagta
taaatagaaaagagaagtggtccaaggactcagctctacatcagaggtcaaagagacaagatggagactag
gagatatgaaggcttatgacagtgagtttgcggagaaacgaagaaacttcccagaagaaaggagaggtcaac
tgctaacaagtcaagtgaaatgagaactgggaaatgagttgacaagagcaatttggctggcggtgatcagaga
atgtttaagagataatgtgaggggaagaaaatggaggcaggaagttgaactactcttttgagtcatttga
aaggaaaaaatggggtgattttactcttttttttttaagataggaaaaaaagtatatattatgctg
aggagaagaatccagttgaagggaataactgtggcttcaggagacagggaaaactgcctaagccacatccttc
agcaagtgaagtttcaagtgagggtttgtctttgcttggggcacgggcttcatccacagtgaaaggaga
gaaggcagggcatgtggggttggctgtagaaagcgggcagacggggtgggaacttatgaagactcttctgat
tggtattttctctgttaagtaaaaggaaaggtcattggctaagaatgaagatggacgcaggttgctgggag
tcatcgaagagaatgaaagaatgaataaaaatagagaaaaatacaatgctattatataaacctatacatattaa
ttactttcctcttcaaattagacccctggaaggcaaatctctgtcatgttaagtttttaggaaaagtcata
atctacttggagctaaagtatgaagaataaggtatatgatttaaacacataaattctatttttgcctaaaccg
gggaagcctttaaggttaacgtagagtgatccattaaaaaagataaaaaatgtcagcttccccttcccttaa
atatagtaaggctcaaaggtaattgatgttcataaccctaaaggtactataacagttctgaagcaaaatattaa
atgtcttctgtagtatttttagttaacttttaattttatttggttaatttatgtgtagtttaaccacatacttg
cctcaactatttcacataaatgtgagatgtcttaggcctctttgaactctgcatggaaaagaatgctgagga
ggatgtctgttttaagctgccactgcctgcctctcataaataatctctcacattgcataaatagcccagataa
actgcagatcgcttagagcctgataaatgagaggaaactgtacagtttgttttccaaattgccttggacag
ctaattcacaatttactattttatagctgtaagattttaaaaatataaaaataacatagctgtaaaacagat
tatcagaagatagttctgtaaaaatgtaaatataatataagctgtaaaatatacactatcggaagtaccaaact
agtttttagtaggttagggcatcaagtaaaaatggaaatgaaagatgtttcaaggaaaactccaggacatctgt
ggcagttactaaagaaaccttcccttctcaggttcccagcatgctattttattgatgtaacaacattttcaata
aagttggtaaatatcactatattactgtcttatagcaacatagcaagagcttttagagatcatataagtata
aaatgtgaattttaaaaaaacaatgaatatgcaggatttttattagggcaagcgtttccataaccataaatat
ttctttaaaaacaaataaatgtcccaagatctctgttagtgatccaaactaagtagaaattagtaaaattaat
tataaatgaacaattttcagcatataaaaccaacaagtcctttctagatttttaacactgtgacccaattgcat
tattttccaagttagaatgactaataatcaatgaatgtaaaagcaataattataacagatgacattgtactt
ttccacagtaaaagaaataaaacaacttaatttttataaaatccattttatatcacaaaataacctttacta
agcaaattttttttaaatctcaggaactatagacatgatgaaaagatagataattttatataaaataattcaaa
aatactgtcagggaaggaaatgtaaaatccttatttgagtaaaagaaaatgctataaagcaatgagttatca
aaatacagaagaggtatttcaaaacaaatgaaaaaccaagatgatgaaatagtgacaactacttctaatgtg
taacagatactgaaatgccaaaggtgaaagtgaactgaattattttcttaaagcagtgaggagaatgtgaacttt
caaaaaatgcaagaagcacagcaaatcaactaattaccacctccttcaataaaaagcgagaacctctt
gggagaattttaagcaccattagcagacacatcttagagc

Figure 2A SEQ ID NO: 5

MACWPQLRLLLWKNLTFRRRQTCQLLLEVAWPLFIFLILISVRLSYPPYEQHECHFPNKAMPSAGTLPWVQ
GIICNANNPCFRYPPTGEPAGVVGNFNKSIVARLFSDDARRLLLSQKDTSMKDMRKVLRTLQOIKKSSSNL
KLQDFLVDNETFSGFLYHNLSLPKSTVDKMLRADVILHKVFLQGYQLHLTSLCNGSKSEMIQLGDQEVSE
LCGLPREKLAAAERVLRNMDILKPIILRTLNSTSPFPSEKELAEATKTLHSLGTLAQELFSMRWSDMRQE
VMFLTNVNSSSSSTQIYQAVSRIVCGHPEGGLKIKSLNWYEDNNYKALFGGNGTEEDAETFYDNSTTPYC
NDLMKNLESSPLSRIIWKALKPLLVGKILYTPDTPATROVMAEVNKTFOELAVFHDLEGMWEELSPKIWTF
MENSQEMDLVRMLLDSRDNDHFWEQQLDGLDWTADQDIVAFLAKHPEDVQSSNGSVYTWEAFNETNQAIRT
ISRFMECVNLNKLPIATEVWLINKSMELLDERKFWAGIVFTGITPGSIELPHHVKYKIRMDIDNVERTNK
IKDGYWDPGRADPFEDMRYVWGGFAYLQDVVEQAIIRVLTGTEKKTGVYMQMPYPCYVDDIFLRVMSRS
MPLFMTLAWIYSVAVVIKGIYVEKEARLKETMRIMGLDNSILWFSWFISSLIPLLVSAGLLVVILKLGNNL
PYS DPSVVFVFLSVFAVVITLQCFLISTLPSRANLAAACGGIYFTLYLPYVLCVAWQDYVGFTLKFASL
LSPVAFGFGCEYFALFEEQIGVQWQDNLFESPVEEDGFNLTSVSMMLFDTFLYGVMTWYIEAVFPQGYGI
YEGQITSFLGHNGAGKTTTMSILTGLFPPTSGTAYILGKDIRSEMSTIRQNLGVCPOHNVLFDMLTVEEHI
WIFYARLKGLSEKHVKAEMEOMALDVGLPSSKLKSKTSQLSGGMQRKLSVALAFVGGSKVILDEPTAGVDP
YSRRGIWELLKRYRQRTIILSTHMDVGLDRIAIISHGKLCVGSLSFLKNQLGTGYLLTLVKKDVE
SSLSSCRNSSSTVSYLKEDSVSQSSSDAGLGSDESHTLTIDVSAISNLIRKHVSEARLVEDIGHELTIV
LPYEAKEGAFVELFHEIDRLSDLGISSYGISETTLEEIFLKVAEESGVDAETSDGTLPARNRRAFGDK
QSCLRPFTEDDAADPNDSIDPESRETDLLSGMDGKSYQVKGWKLQQQFVALLWKRLLIARRSRKGGFA
QIVLPVAVFVCIALVFLIVPPFGKYPSLELQPMYNEQYTFVSNDAEDTGTLELLNALTDPGFGTRCME
GNPDPDTPCQAGEEWTAPVPQTIMDLFQNGNWTMNPSPACQCSSDKIKKMLPVCPGAGGLPPPQRKQ
NTADILQDLTGRNISDYLKTYVQIIAKSLKNKIWNNEFRYGGFSLGVSNTQALPPSQEVNDAIKOMKHL
KLAKDSSADRFLNSLGRFMTGLDTRNNVWVFNKGVHAISSFLNVINNAILRANLQKGENPSHYGITAFN
HPLNLTKQQLSEVALMTTSVDVLVSICVIFAMSFVPASFVVFLIQERVSKAKHLQFISGVKPVYIWLNSNFV
WDMCNYVVPATLVIIIFICFQOKSYVSSSTNLPVLALLLLLYGWSITPLMPASFVFKIPSTAYVVLTSVNL
FIGINGSVATFVLELFTDNKLNNINDILKSVFLIFPHFCLGRGLIDMVKNQAMADALERFGENRFVSPLSW
DLVGRNLFAMAVEGVVFFLITVLIQYRFFIRPRPVNAKLSPLNDEDEDVRRERQRIIDGGGQNDILEIKEL
TKIYRRKRKPAVDRIKVGIPPGECFGLLGNGAGKSSTFKMLTGDTTVTRGDAFLNKNLSILSNIHEVHQN
GYCPQFDAITELLTGREHVEFFALLRGVPEKEVGKVGWAIKRLGLVKYGEKYAGNYSGGNKRKLSTAMAL
IGGPPVVFLEPTTGMDPKARRFLWNCALSVVKEGRSVVLTSHSMEECEALCTRMAMVNGRFRCLGSGVQH
LKNRFGDGYTIVVRIAGSNPDLPVQDFFGLAFPGSVLKEKHRNMLQYQLPSSLSLARIFSIILSQSKKRL
HIEDYSVSQTTLQVFNFAKDQSDDDLKDLKSLHKNQTVVDVAVLTSFLQDEKVKESYV*

Figure 2B SEQ ID NO: 6

GTCCCTGCTGTGAGCTCTGGCCGCTGCCTTCCAGGGCTCCCGAGCCACACGCTGGGGGTG
CTGGCTGAGGGAACATGGCTTGTGGCCTCAGCTGAGGTTGCTGCTGTGGAAGAACCTCA
CTTTCAGAAGAAGACAAACATGTCAGCTGTTACTGGAAGTGGCCTGGCCTCTATTTATCT
TCCTGATCCTGATCTCTGTTTCGGCTGAGCTACCCACCCCTATGAACAACATGAATGCCATT
TTCCAAATAAAGCCATGCCCTCTGCAGGAACACTTCCTTGGGTTTCAAGGGATTATCTGTA
ATGCCAACAACCCCTGTTTCCGTTACCCGACTCCTGGGGAGGCTCCCGAGTTGTTGGAA
ACTTTAACAATCCATTGTGGCTCGCCTGTTCTCAGATGCTCGGAGGCTTCTTTTATACA
GCCAGAAAGACACCAGCATGAAGGACATGCGCAAAGTTCTGAGAACATTACAGCAGATCA
AGAAATCCAGCTCAAACCTGAAGCTTCAAGATTTCTGGTGGACAATGAAACCTTCTCTG
GGTTCCTGTATCACAACCTCTCTCTCCCAAAGTCTACTGTGGACAAGATGCTGAGGGCTG
ATGTCATTCTCCACAAGGTATTTTGGCAAGGCTACCAGTTACATTTGACAAGTCTGTGCA
ATGGATCAAAATCAGAAGAGATGATTCAACTTGGTGACCAAGAAGTTTCTGAGCTTTGTG
GCCTACCAAGGGAGAACTGGCTGCAGCAGAGCGAGTACTTCGTTCCAACATGGACATCC
TGAAGCCAATCCTGAGAACACTAAACTCTACATCTCCCTTCCCGAGCAAGGAGCTGGCTG
AAGCCACAAAAACATTGCTGCATAGTCTTGGGACTCTGGCCCAGGAGCTGTTCAAGCATGA
GAAGCTGGAGTGACATGCGACAGGAGGTGATGTTTCTGACCAATGTGAACAGCTCCAGCT
CCTCCACCCAAATCTACCAGGCTGTGTCTCGTATTGTCTGCGGGCATCCCGAGGGAGGGG
GGCTGAAGATCAAGTCTCTCAACTGGTATGAGGACAACAATAAAAGCCCTCTTTGGAG
GCAATGGCACTGAGGAAGATGCTGAAACCTTCTATGACAACCTCTACAACCTCCTTACTGCA
ATGATTTGATGAAGAATTTGGAGTCTAGTCTCTTTCCCGCATTATCTGGAAAGCTCTGA
AGCCGCTGCTCGTTGGGAAGATCCTGTATACACCTGACACTCCAGCCACAAGGCAGGTCA
TGGCTGAGGTGAACAAGACCTTCCAGGAAGTGGCTGTGTTCCATGATCTGGAAGGCATGT
GGGAGGAACCTCAGCCCCAAGATCTGGACCTTCATGGAGAACAGCCAAGAAATGGACCTTG
TCCGGATGCTGTTGGACAGCAGGGACAATGACCACTTTTGGGAACAGCAGTTGGATGGCT
TAGATTGGACAGCCCAAGACATCGTGGCGTTTTTGGCCAAGCACCCAGAGGATGTCCAGT
CCAGTAATGGTTCTGTGTACACCTGGAGAGAAGCTTTCAACGAGACTAACCAGGCAATCC
GGACCATATCTCGCTTCATGGAGTGTGTCAACCTGAACAAGCTAGAACCCATAGCAACAG
AAGTCTGGCTCATCAACAAGTCCATGGAGCTGCTGGATGAGAGGAAGTTCTGGGCTGGTA
TTGTGTTCACTGGAATTACTCCAGGCAGCATTGAGCTGCCCCATCATGTCAAGTACAAGA
TCCGAATGGACATTGACAATGTGGAGAGGACAAATAAAATCAAGGATGGGTACTGGGACC
CTGGTCTCGAGCTGACCCCTTTGAGGACATGCGGTACGTCTGGGGGGGCTTCGCCTACT
TGCAGGATGTGGTGGAGCAGGCAATCATCAGGGTGCTGACGGGCACCGAGAAGAAAAGT

GTGTCTATATGCAACAGATGCCCTATCCCTGTTACGTTGATGACATCTTTCTGCGGGTGA
TGAGCCGGTCAATGCCCCCTCTTCATGACGCTGGCCTGGATTTACTCAGTGGCTGTGATCA
TCAAGGGCATCGTGTATGAGAAGGAGGCACGGCTGAAAGAGACCATGCGGATCATGGGCC
TGGACAACAGCATCCTCTGGTTTAGCTGGTTCATTAGTAGCCTCATTCTCTCTTGTGA
GCGCTGGCCTGCTAGTGGTCATCCTGAAGTTAGGAAACCTGCTGCCCTACAGTGATCCCA
GCGTGGTGTCTTCTCTCCTGTCCGTGTTTGGCTGTGGTGACAATCCTGCAGTGCTTCCTGA
TTAGCACACTCTTCTCCAGAGCCAACCTGGCAGCAGCCTGTGGGGGCATCATCTACTTCA
CGCTGTACCTGCCCTACGTCTGTGTGTGGCATGGCAGGACTACGTGGGCTTCACACTCA
AGATCTTCGCTAGCCTGCTGTCTCCTGTGGCTTTTGGGTTTGGCTGTGAGTACTTTGCCC
TTTTTGAGGAGCAGGGCATTGGAGTGCAGTGGGACAACCTGTTTGAGAGTCTGTGGAGG
AAGATGGCTCAATCTCACCCTTCGGTCTCCATGATGCTGTTTGACACCTTCCTCTATG
GGGTGATGACCTGGTACATTGAGGCTGTCTTTCCAGGCCAGTACGGAATTCCCAGGCCCT
GGTATTTTCTTGCACCAAGTCCTACTGGTTTGGCGAGGAAAGTGATGAGAAGAGCCACC
CTGGTTCCAACCAGAAGAGAATATCAGAAATCTGCATGGAGGAGGAACCCACCCACTTGA
AGCTGGGCGTGTCCATTGAGAACCTGGTAAAAGTCTACCGAGATGGGATGAAGGTGGCTG
TCGATGGCCTGGCACTGAATTTTTATGAGGGCCAGATCACCTCCTTCCTGGGCCACAATG
GAGCGGGGAAGACGACCACCATGTCAATCCTGACCGGGTGTTCCTCCCGACCTCGGGCA
CCGCCTACATCCTGGGAAAAGACATTGCTCTGAGATGAGCACCATCCGGCAGAACCTGG
GGGTCTGTCCCCAGCATAACGTGCTGTTTGACATGCTGACTGTGGAAGAACAATCTGGT
TCTATGCCCCGCTTGAAAGGGCTCTCTGAGAAGCACGTGAAGGCGGAGATGGAGCAGATGG
CCCTGGATGTTGGTTTGCCATCAAGCAAGCTGAAAAGCAAAACAAGCCAGCTGTGAGGTG
GAATGCAGAGAAAGCTATCTGTGGCCTTGGCCTTGTGCGGGGATCTAAGGTTGTCTTC
TGATGAACCCACAGCTGGTGTGGACCCTTACTCCCGCAGGGGAATATGGGAGCTGCTGC
TGAAATACCGACAAGGCCGCACCATATTCTCTCTACACACCACATGGATGAAGCGGACG
TCCTGGGGGACAGGATTGCCATCATCTCCCATGGGAAGCTGTGCTGTGTGGGCTCCTCCC
TGTTTCTGAAGAACCAGCTGGGAACAGGCTACTACCTGACCTTGGTCAAGAAAGATGTGG
AATCCTCCCTCAGTTCCTGCAGAAACAGTAGTAGCACTGTGTCTATACCTGAAAAAGGAGG
ACAGTGTCTCTCAGAGCAGTTCTGATGCTGGCCTGGGCAGCGACCATGAGAGTGACACGC
TGACCATCGATGTCTCTGCTATCTCCAACCTCATCAGGAAGCATGTGTCTGAAGCCCCGGC
TGGTGGAAGACATAGGGCATGAGCTGACCTATGTGCTGCCATATGAAGCTGCTAAGGAGG
GAGCCTTTGTGGAACCTCTTTCATGAGATTGATGACCGGCTCTCAGACCTGGGCATTTCTA
GTTATGGCATCTCAGAGACGACCCTGGAAGAAATATTCCTCAAGGTGGCCGAAGAGAGTG

GGGTGGATGCTGAGACCTCAGATGGTACCTTGCCAGCAAGACGAAACAGGCGGGCCTTCG
GGGACAAGCAGAGCTGTCTTCGCCCCGTTCACTGAAGATGATGCTGCTGATCCAAATGATT
CTGACATAGACCCAGAATCCAGAGAGACAGACTTGCTCAGTGGGATGGATGGCAAAGGGT
CCTACCAGGTGAAAGGCTGGAACTTACACAGCAACAGTTTGTGGCCCTTTGTGGAAGA
GACTGCTAATTGCCAGACGGAGTCGGAAGGATTTTTTGCTCAGATTGTCTTGCCAGCTG
TGTTTGTCTGCATTGCCCTTGTGTTACGCCCTGATCGTGCCACCCTTTGGCAAGTACCCCA
GCCTGGAACCTTCAGCCCTGGATGTACAACGAACAGTACACATTTGTGAGCAATGATGCTC
CTGAGGACACGGGAACCCCTGGAACCTTTAAACGCCCTCACCAAAGACCCTGGCTTCGGGA
CCCCGTGTATGGAAGGAAACCAATCCCAGACACGCCCTGCCAGGCAGGGGAGGAAGAGT
GGACCACTGCCCCAGTTCCCCAGACCATCATGGACCTCTTCCAGAATGGGAACCTGGACAA
TGCAGAACCCCTTCACCTGCATGCCAGTGTAGCAGCGACAAAATCAAGAAGATGCTGCCTG
TGTGTCCCCCAGGGGCAGGGGGCTGCCTCCTCCACAAAGAAAAACAAACACTGCAGATA
TCCTTCAGGACCTGACAGGAAGAAACATTTTCGGATTATCTGGTGAAGACGTATGTGCAGA
TCATAGCCAAAAGCTTAAAGAACAAGATCTGGGTGAATGAGTTTAGGTATGGCGGCTTTT
CCCTGGGTGTGAGTAATACTCAAGCACTTCCTCCGAGTCAAGAAGTTAATGATGCCATCA
AACAAATGAAGAAACACCTAAAGCTGGCCAAGGACAGTTCTGCAGATCGATTTCTCAACA
GCTTGGGAAGATTTATGACAGGACTGGACACCAGAAATAATGTCAAGGTGTGGTTCAATA
ACAAGGGCTGGCATGCAATCAGCTCTTTCCTGAATGTATCAACAATGCCATTCTCCGGG
CCAACCTGCAAAAGGGAGAGAACCCTAGCCATTATGGAATTACTGCTTTCAATCATCCCC
TGAATCTCACCAAGCAGCAGCTCTCAGAGGTGGCTCTGATGACCACATCAGTGGATGTCC
TTGTGTCCATCTGTGTATCTTTGCAATGTCTTCGTCCCAGCCAGCTTTGTGCTATTCC
TGATCCAGGAGCGGGTCAGCAAAGCAAAACACCTGCAGTTCATCAGTGGAGTGAAGCCTG
TCATCTACTGGCTCTCTAATTTTGTCTGGGATATGTGCAATTACGTTGTCCCTGCCACAC
TGGTCATTATCATCTTCATCTGCTTCCAGCAGAAGTCTATGTGTCTCCACCAATCTGC
CTGTGCTAGCCCTTCTACTTTTGTCTGTATGGGTGGTCAATCACACCTCTCATGTACCCAG
CCTCCTTTGTGTTCAAGATCCCCAGCACAGCCTATGTGGTGTCTACCAGCGTGAACCTCT
TCATTGGCATTAAATGGCAGCGTGGCCACCTTTGTGCTGGAGCTGTTACCCGACAATAAGC
TGAATAATATCAATGATATCCTGAAGTCCGTGTTCTTGATCTTCCCACATTTTGCCTGG
GACGAGGGCTCATCGACATGGTGAAAAACCAGGCAATGGCTGATGCCCTGGAAAGGTTTG
GGGAGAATCGCTTTGTGTACCATATCTTGGGACTTGGTGGGACGAAACCTCTTCGCCA
TGGCCGTGGAAGGGGTGGTGTCTTCTCCTCATTACTGTTCTGATCCAGTACAGATTCTTCA
TCAGGCCCAGACCTGTAAATGCAAAGCTATCTCCTCTGAATGATGAAGATGAAGATGTGA
GGCGGGAAAGACAGAGAATTCTTGATGGTGGAGGCCAGAATGACATCTTAGAAATCAAGG
AGTTGACGAAGATATATAGAAGGAAGCGGAAGCCTGCTGTTGACAGGATTTGCGTGGGCA

TTCTCCTGGTGAGTGCTTTGGGCTCCTGGGAGTTAATGGGGCTGGAAAATCATCAACTT
TCAAGATGTTAACAGGAGATACCACTGTTACCAGAGGAGATGCTTTCCTTAACAAAAATA
GTATCTTATCAAACATCCATGAAGTACATCAGAACATGGGCTACTGCCCTCAGTTTGATG
CCATCACAGAGCTGTTGACTGGGAGAGAACACGTGGAGTTCTTTGCCCTTTTGAGAGGAG
TCCCAGAGAAAGAAGTTGGCAAGGTTGGTGAGTGGGCGATTCCGAAACTGGGCCTCGTGA
AGTATGGAGAAAAATATGCTGGTAACATAGTGAGGCAACAAACGCAAGCTCTCTACAG
CCATGGCTTTGATCGGCGGGCCTCCTGTGGTGTCTTCTGGATGAACCCACCACAGGCATGG
ATCCCAAAGCCCGGCGGTTCTTGTGGAATTGTGCCCTAAGTGTGTCAAGGAGGGGAGAT
CAGTAGTGCTTACATCTCATAGTATGGAAGAATGTGAAGCTCTTGGCACTAGGATGGCAA
TCATGGTCAATGGAAGGTTTCAGGTGCCTTGGCAGTGTCCAGCATCTAAAAAATAGGTTTG
GAGATGGTTATACAATAGTTGTACGAATAGCAGGGTCCAACCCGGACCTGAAGCCTGTCC
AGGATTTCTTTGGACTTGCATTTCTTGGAAAGTGTCTAAAAGAGAAACACCGGAACATGC
TACAATACCAGCTTCCATCTTCATTATCTTCTCTGGCCAGGATATTCAGCATCCTCTCCC
AGAGCAAAAAGCGACTCCACATAGAAGACTACTCTGTTTCTCAGACAACACTTGACCAAG
TATTTGTGAACTTTGCCAAGGACCAAAGTGATGATGACCCTTAAAAGACCTCTCATTAC
ACAAAAACCAGACAGTAGTGACGTTGACGTTCTCACATCTTTTCTACAGGATGAGAAAG
TGAAAGAAAGCTATGTATGAAGAATCCTGTTCATACGGGGTGGCTGAAAGTAAAGAGGAA
CTAGACTTTCTTTGCACCATGTGAAGTGTGTGGAGAAAAGAGCCAGAAGTTGATGTGG
GAAGAAGTAACTGGATACTGTACTGATACTATTCAATGCAATGCAATTCAATGCAATGA
AAACAAAATTCCATTACAGGGGCAGTGCCCTTTGTAGCCTATGTCTTGTATGGCTCTCAAG
TGAAAGACTTGAATTTAGTTTTTTTACCTATACCTATGTGAACTCTATTATGGAACCCAA
TGGACATATGGGTTTGAACCTCACACTTTTTTTTTTTTTTTTGTTCCTGTGTATTCTCATT
GGGGTTGCAACAATAATTCATCAAGTAATCATGGCCAGCGATTATTGATCAAAAATCAAAA
GGTAATGCACATCCTCATTCACTAAGCCATGCCATGCCCAGGAGACTGGTTTCCCGGTGA
CACATCCATTGCTGGCAATGAGTGTGCCAGAGTTATTAGTGCCAAGTTTTTCAGAAAGTT
TGAAGCACCATGGTGTGTCTGCTCACTTTTGTGAAAGCTGCTCTGCTCAGAGTCTATCA
ACATTGAATATCAGTTGACAGAATGGTGCCATGCGTGGCTAACATCCTGCTTTGATTCCC
TCTGATAAGCTGTTCTGGTGGCAGTAACATGCAACAAAAATGTGGGTGTCTCCAGGCACG
GGAACTTGGTTCCATTGTTATATTGTCCTATGCTTCGAGCCATGGGTCTACAGGGTCAT
CCTTATGAGACTCTTAAATATACTTAGATCCTGGTAAGAGGCAAAGAATCAACAGCCAAA
CTGCTGGGGCTGCAACTGCTGAAGCCAGGGCATGGGATTAAAGAGATTGTGCGTTCAAAC
CTAGGGAAGCCTGTGCCCATTTGTCTGACTGTCTGCTAACATGGTACACTGCATCTCAA
GATGTTTATCTGACACAAGTGATTATTTCTGGCTTTTGAATTAATCTAGAAAATGAAA

Figure 3
Promoter, 8797 bp

distances numbered using first base of promoter as 1

Name	Pos. of 1st base in sense strand	Hit Site	% Match	Strand	SEQ ID No.
LXRE		Target: AGGTCA (NNNN)AGGTCA			7
DR4	-7531	AGAGCAGGTGGATCATTTGAGTCA	88	sense	8
DR4	-5085	TTGAGCGCGGTGATCCTTGAGTCA	88	antisense	9
DR4	-4389	CAAGCGGGCAGATCCTTGAGTTA	88	antisense	10
DR4	-1641	CAAGTGGGCGAGTTCACCTCAGTCA	94	antisense	11
DR1		None			
PPAR		Target: NNNNN (A) NN (T) TGACCT (N/NN)TGACCT			12
DR2	-7718	CTTTGA (A) GC (C) TGATCATATGACCT	88	antisense	13
DR2	-7521	AGGCTG (G) TC (T) CGAACTCCTGACCT	88	antisense	14
DR2	-5708	CTTAAT (T) GG (T) GCGCTGTGACCT	91	antisense	15
DR2	-2894	CAGGAT (G) GC (G) TAACTCCTGACCT	88	antisense	16
DR2	-1649	AGGTTG (G) TT (T) CGAACTCCTGACCT	88	sense	17
DR2	-1140	TCAAGG (T) AG (G) AGACCTTGTGGCCT	88	sense	18
DR1		None			

Name	Pos. of 1st base in sense strand	Hit Site	% Match	Strand
Target: ATCACCCCAC				
SREBP	-8523	GAGATGTGCTATGACCCAC	90	antisense
	-3651	GTGAGCCGATCACCAC	90	antisense
	-7747	TCCATCCATCCACACCCAC	80	antisense
	-5485	CCCTTTTATTAAACACCTCAC	80	antisense
	-5248	GTAAGCCAAGATCATGCCAC	80	antisense
	-5073	ACCTCAAGTGATCACCGGCC	80	sense
	-2252	GGCTCAAGCGATCCTCCAC	80	antisense
	-2209	CCATGATTGGATCACTGCAC	80	sense
	-1794	GTGAGTCGAGATCATGCCAC	80	antisense
	-519	TGCTTTTGTTCCTCCAC	80	antisense
	-478	CGGCTTCCCTCAGCCAC	80	sense
	-158	ACCTCCACCCCGACCCAC	80	sense
Target: (W){0,8}WRGGTCA				
ROR	-8435	CTGGGCAAGGATGGGTCA	100	sense
	-8434	TGGGCAAGGATGGGTCA	100	sense
	-7025	AAAAGCACCAGGTCA	100	antisense
	-3989	ACAAGATGCCAGGTCA	100	sense
	-2638	GAGGAGATGGAGGTCA	100	sense

Exon 1, 303 bp

Distances numbered using start of Exon 1 as

Name	Pos. of 1st base in +	Hit Site	% Match	Strand	Q ID NO.
LYRE		Target: AGGTCA (NNNN)AGGTCA			7
DR4	4	CCGAGCGCAGAGGTTACTATCGGTCA	92	antisense	38
DR1		None			

PPAR

DR2

DR1

None

None

SRBP

None

ROR

None

5' Intron 1, 930 bp

Positions numbered using the first position in intron 1 as + 1

Name	Pos. of 1st base in +	Hit Site	Match	Strand	SEQ ID N
LXRE		Target: AGGTCA (NNNN)AGGTCA			7
DR4	458	GCCAAATTCACAGTCAGACACAGCA	88	antisense	39
DR1		None			
PPAR		Target: NNNNN (A) NN (T) TGACCT (N/NN)TGACCT			12
DR2		None			
DR1		None			
SREBP		Target: ATCACCCAC			19
	326	GGACCTGCAGCTCTCCCCAC	80	antisense	40
ROR		Target: (W) {0,8}WRGGTCA			32
	17	AAGCCCAAGTAGTCA	94	antisense	41
	161	GAGCTCGTACTAGGACA	94	antisense	42
	181	GCAGAGTCTCTGGGTCA	94	antisense	43
	181	CGCAGAGTCTCTGGGTCA	94	antisense	44
	478	AGCCAATTCACAGGTCA	94	antisense	45
	559	ACGGACCGTTTGGGACA	94	antisense	46
	559	CACGACCGTTTGGGACA	94	antisense	47
	559	CCACGACCGTTTGGGACA	94	antisense	48
	589	ACTAGAGCGCTTGGGTCT	94	sense	49
	590	CTAGAGCGCTTGGGTCT	94	sense	50
	612	CCCTACCCCTCAGGTCA	94	antisense	51
	612	TCCTACCCCTCAGGTCA	94	antisense	52
	668	GSTCTGCCAGGAGACA	94	antisense	53
	864	TTTTAGTGAGANGGTTA	94	sense	54

Positions numbered using the first base as -1 to the start of Exon 2 as -1

Name	Pos. of 1st base in +	Hit Site	Mat	Strand
Target: AGGTCA (NNNN)AGGTCA				
LXRE				7
DR4	-7188	TGAGGAGGTAGATCACTTGAGGTCA	93	sense
DR4	-11050	CGAGGCTGGCGGATCACTTGAGGTCA	86	sense
DR4	-7670	AAGCCTAACAGGTACTGAGGCCA	86	antisense
DR4	-4696	AGAGGTGGCGGATCACCTGAGGTCA	86	antisense
DR1		None		
Target: NNNNN (A) NN (T) TGACCT (N/NN) TGACCT				
PPAR				12
DR1		None		
DR2	-10281	CTCGAT (T) TC (C) TGACCTCGTGATCC	86	antisense
DR2	-5996	CAAAAC (A) TT (G) TGCCCTTTTGAAT	86	antisense
DR2	-932	GCGCTA (G) G3 (T) TGTCTCTATTACCT	86	sense
DR2	-597	CTCGAT (T) TC (T) TGACCTCGTGATCC	86	sense
Target: ATCACCCAC				
SREBP				19
	-7009	GTGAGCTGAGATCAACCCAC	90	sense
	-11869	TTCAAGGATGATCACCACAT	80	antisense
	-11616	GGCTCAAGTGATCTCTCCAC	80	antisense
	-10100	GTGAGCCGAGATCGGCCAC	80	sense
	-8584	GTGAGTTATGATCATGCCAC	80	antisense
	-5591	CCACTGTTTGAACACCCAC	80	sense
	-4684	ACCTCAGGTGATCCGCCAC	80	sense
	-4128	AAATGTGACATCTCCACAC	80	antisense
	-2524	AATATAGATATCAGCTCC	80	antisense
	-1577	CCTTTTATCTACCCACAC	80	antisense

base in +		Target: (W{0,8}WRGGTCA		
ROR				32
-12418	CCTTGTGGATGGGTCA	100	antisense	73
-12418	GCCTTGTGGATGGGTCA	100	antisense	74
-11947	TTGCTGTGAGTGGGTCA	100	antisense	75
-7976	GCCTTGCAAGAGGGTCA	100	antisense	76
-7976	GGCCTTGCAAGAGGGTCA	100	antisense	77
-7789	ATTAAAGCTGATGGGTCA	100	sense	78
-7788	ATTAAGCTGATGGGTCA	100	sense	79
-5934	AGGTGCTAACTAGGGTCA	100	sense	80
-5933	GGTGTCTAACTAGGGTCA	100	sense	81
-4509	ATGGGATGACTGGGTCA	100	sense	82
-1538	TCTCCATGCCAAGGTCA	100	antisense	83

Coding Polymorphisms (cSNP)									
Exon	Numbering based on PubMed AJ012374.1 et al. 2000	Numbering	Sequence	Change in codon	Coding Nucleotide Change	AA change	Genotype	ML16	ML18
Exon 05/UT	89	NA	GGAACTAGTCCGCGGAAA	NA	C8T	Not applicable	CC	CC	CC
Exon 05/UT	127	NA	GGAACTAGTCCGCGGAAA	NA	C127G	Not applicable	CC	CC	CC
Exon 06/UT	319	(-) 258	CCGGAGGCGGAGAGCC	NA	Ins319	Not applicable	NA	NA	NA
Exon 06/UT	378	(-) 188	ACACGCTGGCGGTGCTGGCTG	NA	G378C	Not applicable	NA	NA	NA
Exon 5	880	414	CTGGCTTCCTGATTCAGACG	CTG-CTA	G880A	No aa change	NA	NA	NA
Exon 5	931	598	GGCTTACCAAGGAGGAGCTG	AGG-AAG	G1051A	R218K	NA	NA	NA
Exon 5	1331	870	GGCGGATCCCGGAGGAGGAGG	GGG-GGA	C1331T	No aa change	NA	NA	NA
Exon 5	1343	886	AGGAGGCGGAGGAGGAGGAGG	GGG-GGA	G1343A	No aa change	NA	NA	NA
Exon 10	1591	1138	TCAGTCCAGGCGGAGGAGGAGG	GTG-GGG	T1591C	V388A	NA	NA	NA
Exon 16	2708	2281	GGAGGAGTACGTTGGGTTTAC	GTT-ATG	G2708A	V771L	NA	NA	NA
Exon 15	2715	2280	GGTGGGCTTCGAGTCAAGAT	ACA-CCA	A2715C	T774P	NA	NA	NA
Exon 15	2723	2288	TCACATCAACATCTTGGCTG	AAG-AAC	G2723C	K776N	NA	NA	NA
Exon 16	2808	2413	CCACTGCGGTTGCGATG	GTC-ATC	G2808A	V828L	NA	NA	NA
Exon 17	3044	2588	GAGAGGATATCAGAAAG	ATG-ATG	A3044G	H83M	NA	NA	NA
Exon 21	3654	3099	GATGTAGGTTGCTATCTGG	GTT-GTG	T3594G	No aa change	NA	NA	NA
Exon 23	3911	3458	GGGACATGAGAGTGAAGG	GAG-GAG	G3911C	E1172D	NA	NA	NA
Exon 34	5155	4700	CTGGACACGAGAAATATGTC	AGA-AAA	G5155A	R1587K	NA	NA	NA
Exon 37	5587	5132	TGCTATGTTGCTCCACCAT	TGC-TGC	C5587G	S1731C	NA	NA	NA

[illegible]

Non-coding Polymorphisms (SNP)		Numbering based on Pullinger et al., 2000	Sequence	Change in non-coding	Coding	AA change	Genotypes																				
Intron																											
Promoter		(-181)	NA	Variant																							
Promoter		(-117)	NA	Variant																							
Intron 0		(-1183)	(-1425)	Wildtype																							
Intron 0		(-1185)	(-1387)	Wildtype																							
Intron 0		(-1827)	(-1229)	Wildtype																							
Intron 0		(-1728)	(-982)	Wildtype																							
Intron 0		(-1481)	(-1733)	Wildtype																							
Intron 0		(-1382)	(-1354)	Wildtype																							
Intron 7		(-2383)	(-2383)	Polymorph																							
Intron 7		(-3035)	(-3035)	Polymorph																							
Intron 7		(-115)	(-115)	Wildtype																							
Intron 9		(-142)	(-142)	Wildtype																							
Intron 13		(-24)	(-24)	Wildtype																							
Intron 13		(-83)	(-83)	Wildtype																							
Intron 15		(-4.5)	(-4.5)	Wildtype																							
Intron 17		(-2000)	(-2000)	Polymorph																							
Intron 21		(-118)	(-118)	Polymorph																							

[illegible]

Errors in public sequence (differences between all samples and Genbank entry AJ012378.1):									
Exon/intron	Numbering based on Pullinger et al., 2000	Numbering based on	Sequence difference/contast in cDNA	Change in codon or non-coding	Coding Nucl. Change	AA change	Genotypes	HL18	HL20
							ABE MGA ALA	212	BC11 BAC
Exon 2	16, 18	Public seq Correct seq	TGTCAGCTGTTACTGGAGTGG TGTCAGCTGCTGCTGGAGTGG	T to C: A to G		No aa change		Present in all samples tested	
Exon 7	705	Public seq Correct seq	AGGAGCTGGCCGAGGCGACAA AGGAGCTGGCTGAGGCGACAA	C to T		No aa change		Present in all samples tested	
Exon 33	4804	Public seq Correct seq	ATGATGCGACCAACAAATG ATGATGCGATCAACAAATG	A to C: ATC		Thr to Ile		Present in all samples tested	
Exon 35	4803	Public seq Correct seq	GAGGTGGCTGGGATGACCA GAGGTGGCTGTGATGACCA	CGC to TG		Pro to Leu		Present in all samples tested	
Exon 43	5851	Public seq Correct seq	TTCCTTACAGAAATAGTATC TTCCTTACAGAAATAGTATC	AGA to AAA		Arg to Lys		Present in all samples tested	
Exon 48	6443	Public seq Correct seq	GGAAAGTGTTCMAAAGAGAAA GGAAAGTGTTCMAAAGAGAAA	CGA to CTA		Pro to Leu		Present in all samples tested	
Exon 49	6765	Public seq Correct seq	AGTAAAGAGGAGTAGACTTT AGTAAAGAGGAGTAGACTTT	G to A		No aa change		Present in all samples tested	

Figure 5A

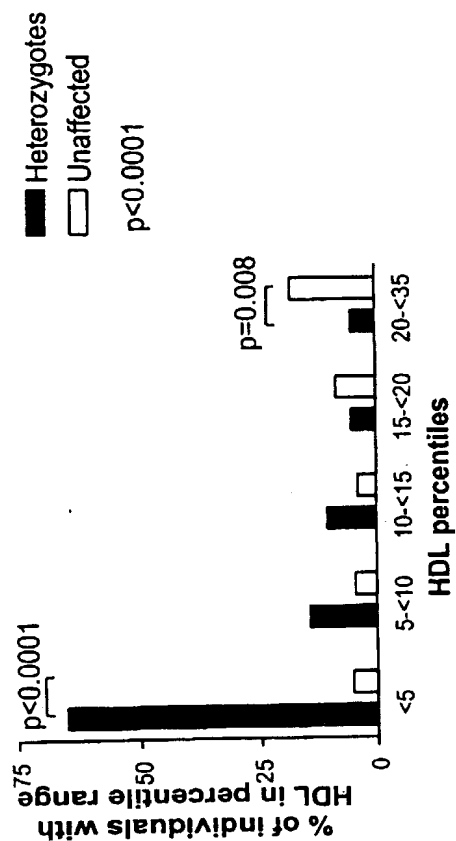


Figure 5B

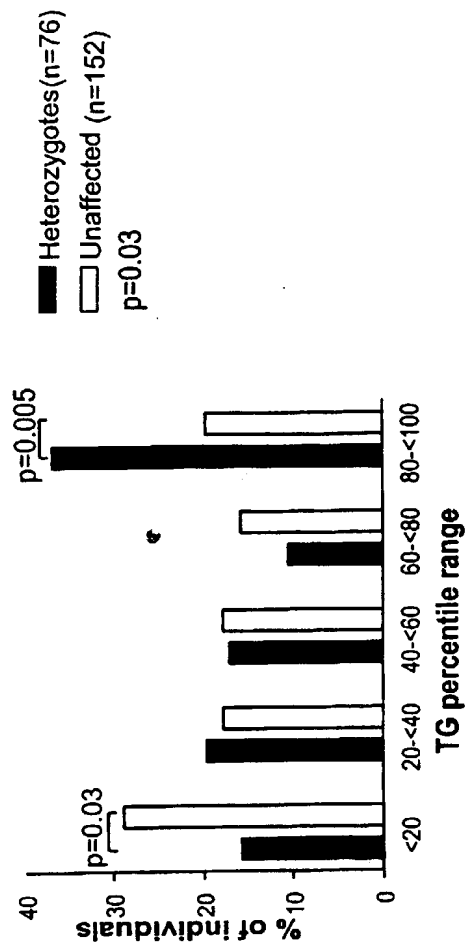


Figure 6

	TD Patients	Heterozygotes	Unaffected family members	P-value heterozygotes vs. unaffected	P-value TD patients vs. unaffected
number	5	77 ^A	156 ^A		
age (yrs) range	43.4±9.0 31-56	42.5±19.6 5-81	39.9±21.0 4-86	0.35	0.71
m/f	3/2	33/44	82/74	0.16	0.74
TC (mmol/L)	2.34±1.03	4.52±1.12	4.71±1.07	0.23	<0.0001
TG (mmol/L)	1.95±0.97	1.66±1.59	1.20±1.03	0.03	0.11
HDL (mmol/L)	0.08±0.05	0.74±0.24	1.31±0.35	<0.0001	<0.0001
LDL (mmol/L)	1.37±1.02	3.03±0.99	2.84±0.87	0.171	0.0003
ApoA-I (g/L)	0.03±0.04 (3)	0.92±0.32 (61)	1.43±0.26 (55)	<0.0001	<0.0001
ApoA-II (g/L)	0.10±0.08 (2)	0.35±0.08 (46)	0.39±0.08 (43)	0.01	<0.0001
ApoB (g/L)	0.89±0.53 (2)	0.93±0.25 (52)	0.94±0.33 (42)	0.88	0.84
CHD ≥ 20 yrs	20% (1/5)	12.9% (8/62)	4.1% (5/122)	0.03	0.10
Odds Ratio (95% CI)				3.47 (1.08-11.09)	5.85 (0.55-62.4)
Age of onset	38	48.9±8.6	60.4±12.8	0.08	

^A For TC, TG, LDL n=76 for heterozygotes, 153 for unaffected family members

Figure 7

Individual	Mutation	exon	disease (age of onset)
TD proband			
TD1	C1477R, ivs24+1G-->C 30, intron 24		CHD (38)
ABC1 heterozygotes			
TD4-201	unidentified	-	MI (<58)
FHA5-215	M1091T	22	MI (61)
FHA5-303	M1091T	22	CHD (<45)
TD1-363	C1477R	30	MI (51)
FHA3-301	Del(E,D) 1893,94	41	PVD (<54)
FHA3-305	Del(E,D) 1893,94	41	CHD (44)
FHA6-201	P2150L	48	CVA (36), fatal MI (58)
FHA2-301	R2144X	48	CAD (42), PTCA (47), femoral angioplasty (48), CABG (<50)
Unaffected family members			
FHA5-212	none	-	AP (62)
TD3-109	none	-	TIA (80)
FHA2-315	none	-	MI (51)
TD1-205	none	-	MI (62)
TD1-216	none	-	AP (47)

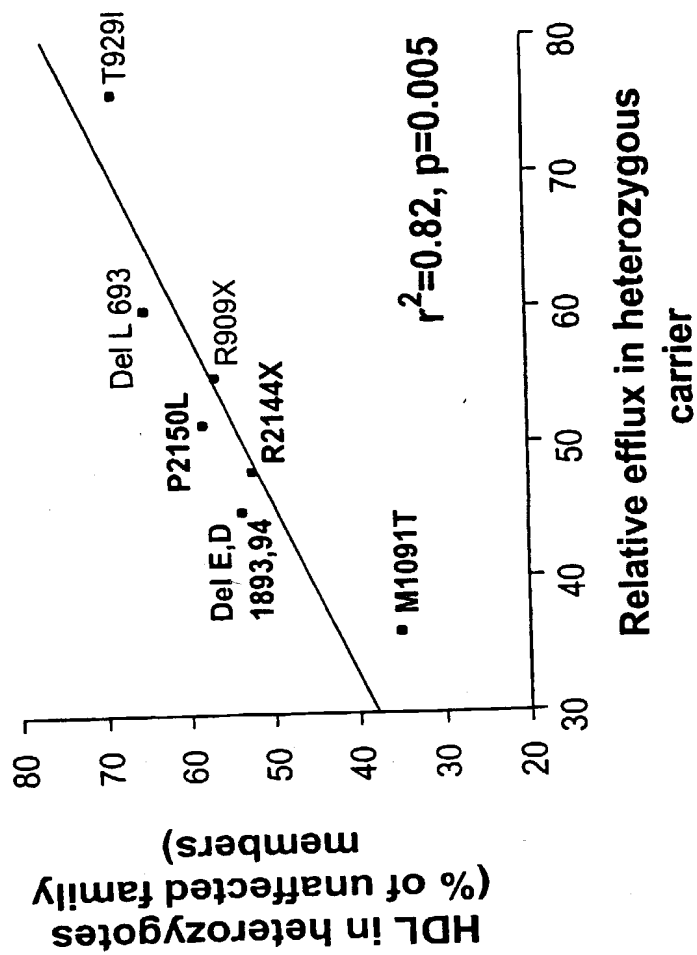


Figure 8

Figure 9

family	mutation	HDL in		HDL in unaffected		HDL in		Age and sex matched		CAD in
		heterozygotes	mean \pm SD (n)	family members	heterozygotes	heterozygotes	% of unaffected	population median ^A	heterozygotes	
FHA1	Del L 693	0.79 \pm 0.20 (8)	1.22 \pm 0.35 (11)		64.8			1.39 \pm 0.08	-	
FHA2	R2144X	0.56 \pm 0.23 (12)	1.07 \pm 0.22 (20)		52.3			1.34 \pm 0.19	+	
FHA3	Del E,D 1893,94	0.77 \pm 0.24 (8)	1.44 \pm 0.38 (9)		53.5			1.30 \pm 0.17	+	
FHA4	R909X	0.59 \pm 0.26 (5)	1.04 \pm 0.37 (9)		56.5			1.39 \pm 0.24	-	
FHA5	M1091T	0.48 \pm 0.48 (4)	1.37 \pm 0.43 (6)		35.0			1.56 \pm 0.05	+	
FHA6	P2150L	0.61 \pm 0.07 (7)	1.05 (1)		58.1			1.30 \pm 0.22	+	
TD1	ivs25+1G-->C	0.78 \pm 0.06 (4)	1.35 \pm 0.29 (70)		57.8			1.22 \pm 0.22	-	
TD4	del C 6825-->2145X	0.91 \pm 0.10 (2)	1.00 \pm 0.05 (3)		91.0			1.31 \pm 0.16	-	
TD5	CTC6952-4TT-->2203X	0.80 \pm 0.20 (3)	1.65 (1)		48.5			1.39 \pm 0.19	-	
TD1	C1477R	0.82 \pm 0.18 (9)	1.35 \pm 0.29 (70)		60.7			1.37 \pm 0.14	+	
TD2	Q597R	0.82 \pm 0.07 (5)	none available		-			1.39 \pm 0.17	-	
TD3	T929I	1.01 \pm 0.18 (8)	1.48 \pm 0.42 (26)		68.2			1.33 \pm 0.19	-	
TD4	unidentified	0.74 \pm 0.05 (2)	1.00 \pm 0.05 (3)		73.5			1.49 \pm 0.09	+	

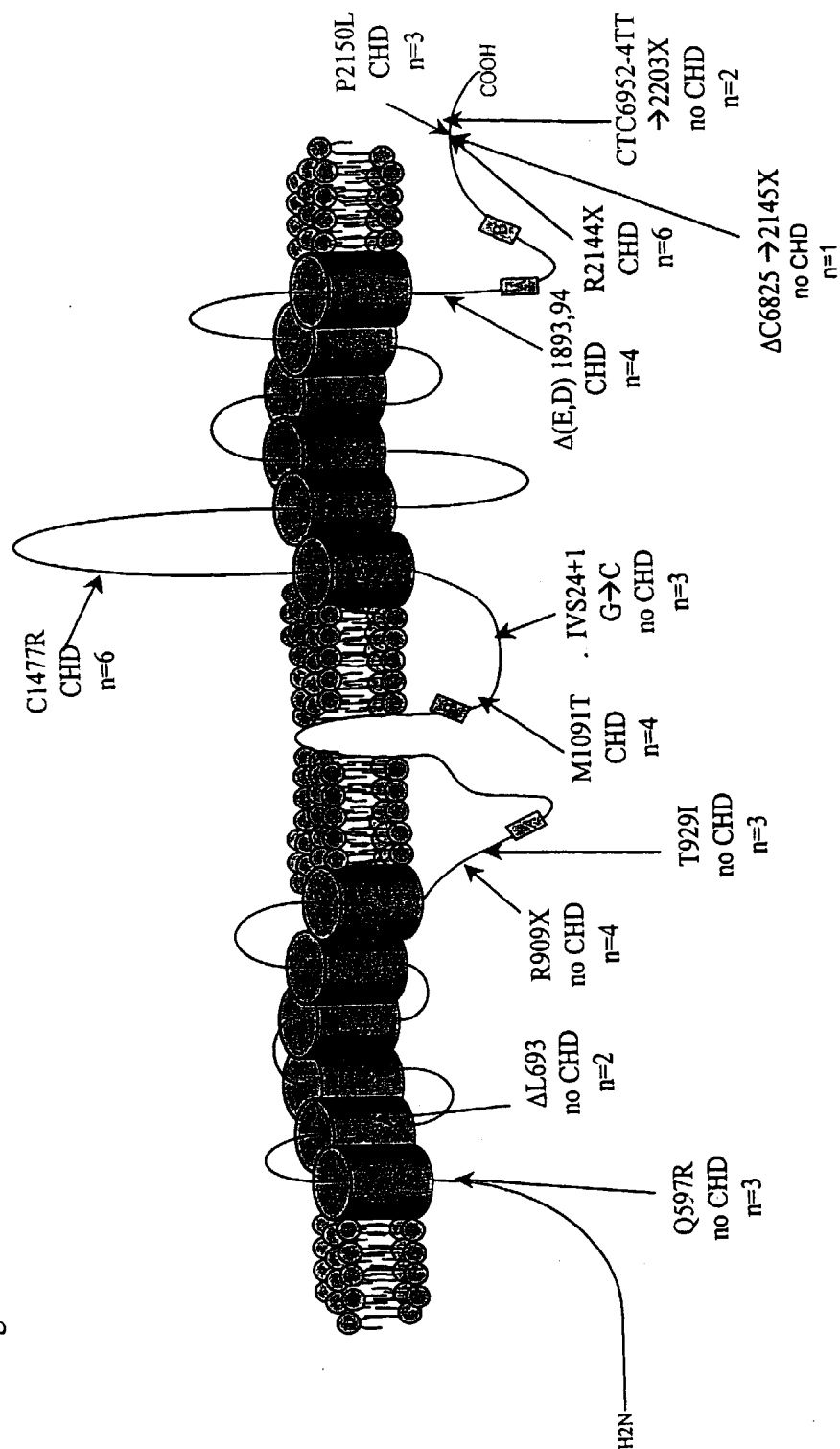
^A Calculated based on mean the age and sex specific 50th percentile levels in the LRC population

Figure 10

	Missense	Severe	P-value	Unaffected	P-Value	P-value
	Mutations	Mutations	Missense vs.	Controls	Missense vs.	Severe vs.
	(n=33)	(n=42) ^A	Severe	(n= 156)	unaffected	unaffected
TC (mmol/L)	4.78±1.30	4.30±0.95	0.08	4.71±1.07	0.76	0.02
TG (mmol/L)	1.77±2.15	1.55±1.01	0.58	1.20±1.03	0.14	0.06
HDL (mmol/L)	0.78±0.26	0.70±0.23	0.18	1.31±0.35	<0.0001	<0.0001
LDL (mmol/L)	3.19±1.10	2.90±0.91	0.23	2.84±0.87	0.10	0.73

^A for TC, TG, LDL measurements, n=41 for severe mutations, 153 for unaffected

Figure 11



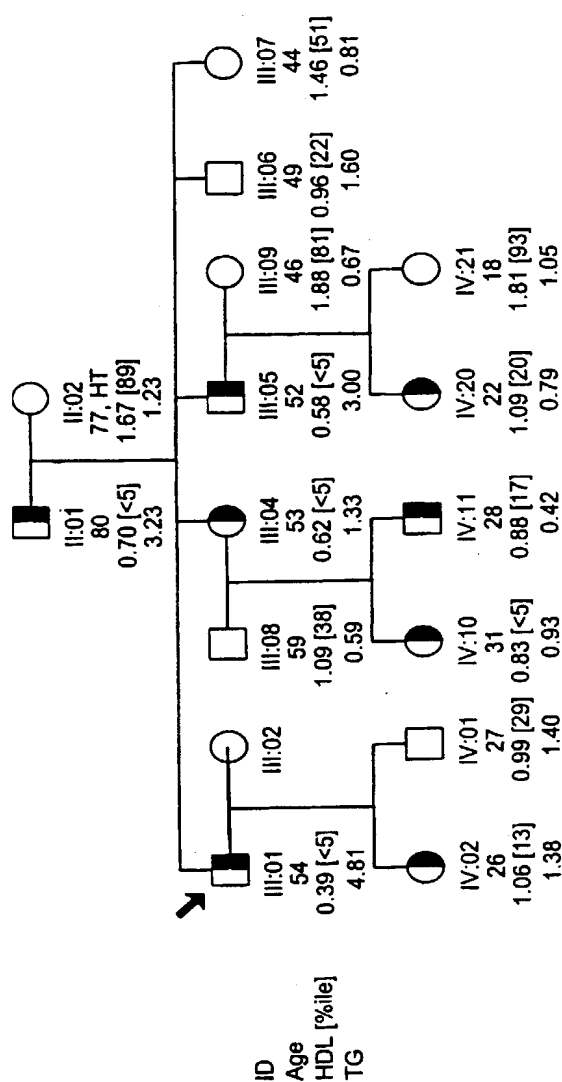


Figure 12A.

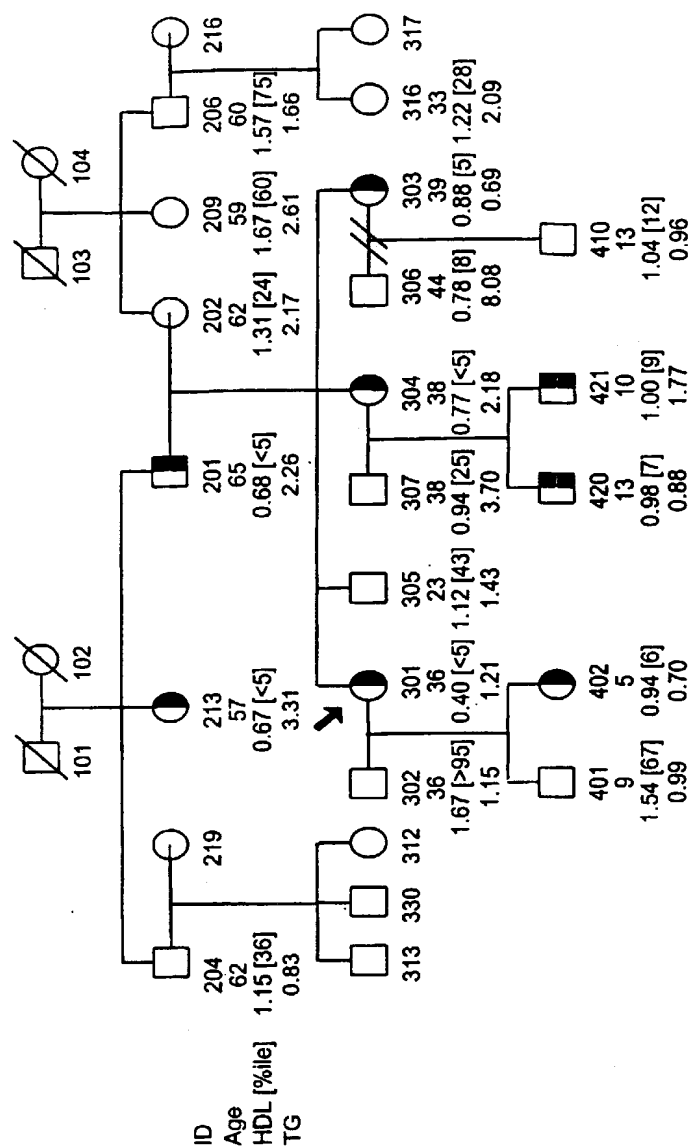


Figure 12B.

71/86

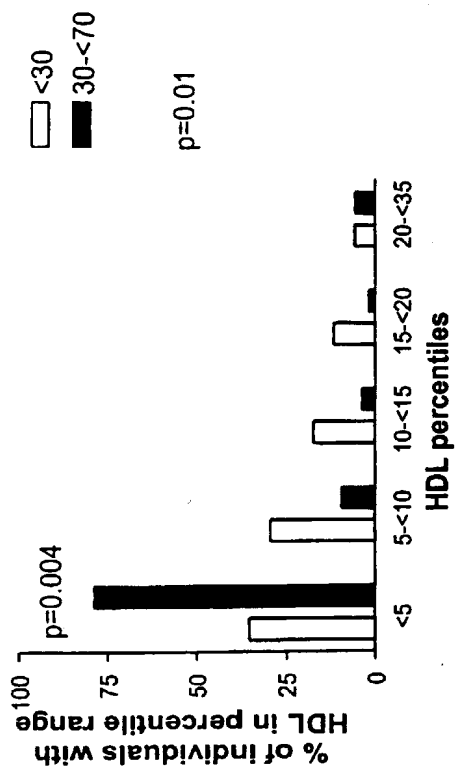


Figure 13

Figure 14

	Heterozygotes	Unaffected	P-value Heterozygotes
	mean±SD (n)	mean±SD (n)	vs. Unaffected
HDL (mmol/L)			
<30	0.91±0.16 (17)	1.26±0.29 (51)	<0.0001
≥30	0.66±0.24 (52)	1.32±0.36 (90)	<0.0001
Change	-0.25	+0.06	0.21
p-value <30 vs. ≥30	0.0002	0.23	
TG (mmol/L)			
<30	1.07±0.96 (16)	0.88±0.45 (51)	0.26
≥30	1.84±1.79 (52)	1.36±1.24 (87)	0.07
Change	+0.77	+0.48	0.97
p-value <30 vs. ≥30	0.03	0.001	

Figure 15A

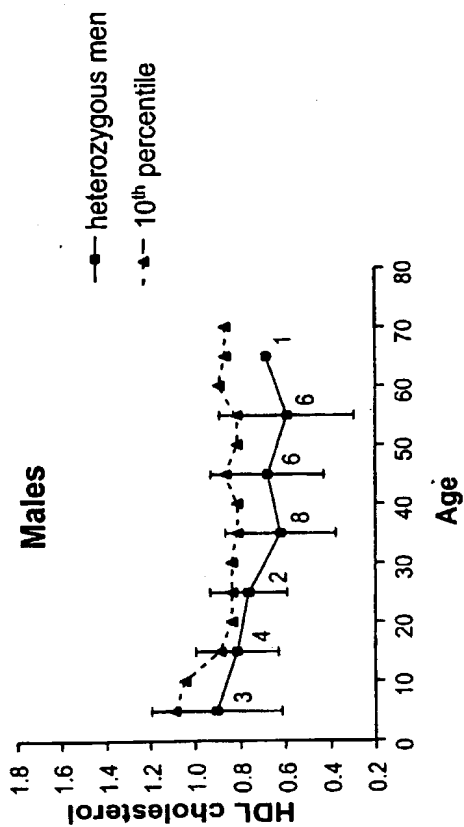


Figure 15B

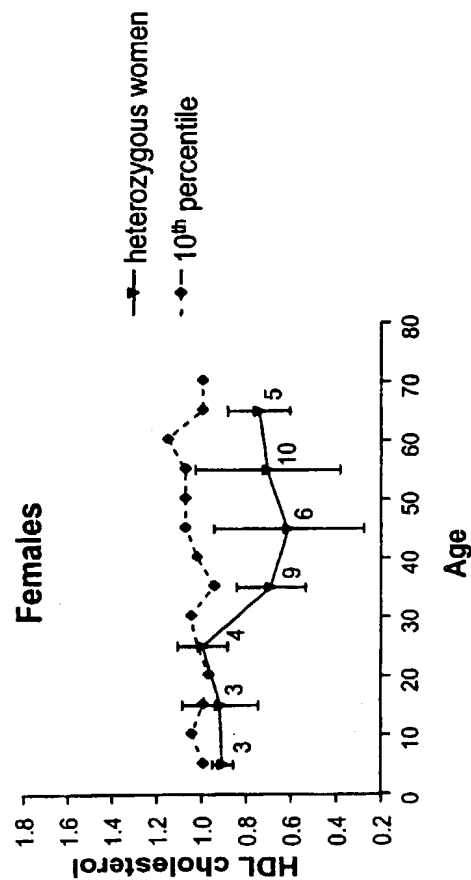


Figure 16A

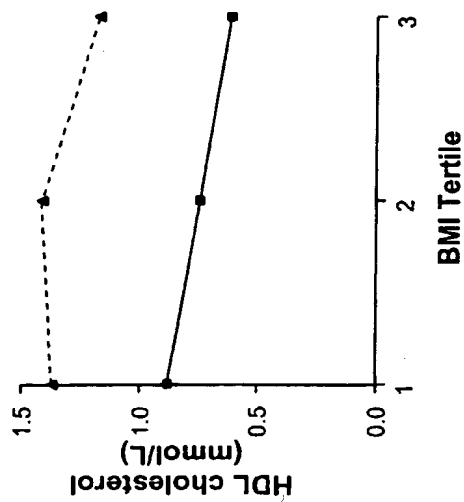


Figure 16B

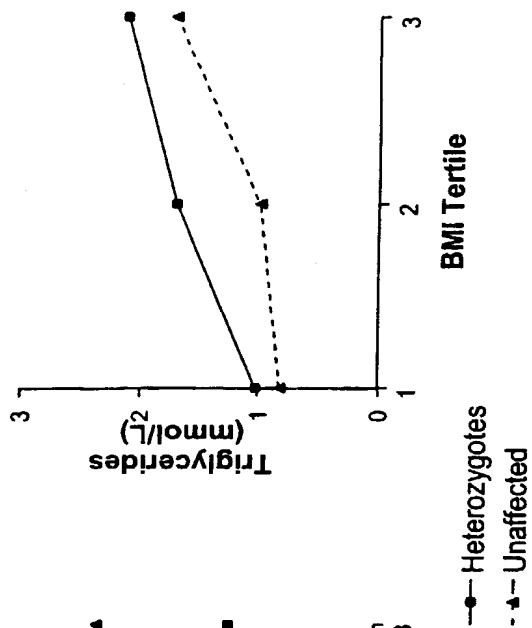


Figure 17

Variant	Amount of each dNTP (μ M)	Pmol each oligo	Forward oligo (5'→3') ^a Reverse oligo (5'→3') ^a	Annealing temp. (C)	Enzyme	Products (bp): wt "A" allele variant "B" allele	SEQ ID No:
G1051A (R219K)	187.5	20	GTATTTTGCAAGGCTACCAAGTTACATTTTGACAA GATTGGCTTCAGGATGTCCTGTTGGAA	60	EcoN I	177 107,70	211 212
T1591C (V399A)	200	27.5	GCTGCTGTGATGGGGTATCT ACCTCACTCACACCTGGGAA	57	Hph I	117,103,48,33 220,48,33	213 214
G2706A (V771M)	200	27.5	CAAGTGAGTGCTTGGGATTG TGCTTTTATTCAGGGACTCCA	57	BsaA I	98,252 350	215 216
A2715C (T774P)	200	27.5	GTGATCCCAGCGTGGTGTGTTGCTT GAAAGGCCAGAGGTACTCACAGCGAAGATCTTGAGGG	55	Hph I	56,69,95 56,161	217 218
G2723C (K776N)	187.5	12	TCGTTTTTATTCAGGGACTCCA CAAGTGAGTGCTTGGGATTG	55	Bgl II	269,80 349	219 220
G2868A (V825I)	200	27.5	CCCATGCACCTGCAGAGATTG GCAAATTCAAATTTCTCCAGG	57	Bsa I	149,237 386	221 222
A3044G (R83M)	200	27.5	GAGAAGAGCCACCTGTTCCAAACAGAGAGGAI AAGGCAGGAGACATCGCTT	55	EcoR V	94,35 129	223 224
G3911C (E1172C)	200	27.5	GAGCAGTCTGATGCTGGCCTGGGCGAGGCCACCGA TCTGCACCTCTCCTCCTCTG	55	BssS I	104,37 141	225 226
G5155A (R1587K)	200	27.5	CAGCTTGGGAAGATTATGACAGGACTGGACACGA ATGCCCTGCCCACTTAC	55	BssS I	114,31 145	227 228
C5587G (S1731C)	187.5	20	GTGCAATTACGTTGTCCTGCCACACT CCATACAGCAAAAGTAGAAGGGCTAGCACA	60	Mnl I	82,35 117	229 230
G(-191)C	187.5	24	CAGCGCTTCCCGCGGCTCTTAG CCACTCACTCTCGTCCGCAATTAC	60	HgaI	287,55,3 342,3	233 234

C(-17)G	187.5	18	CTGCTGAGTGAAGTAAACAGAGGCGGGTA CCACTCACTCTCGTCCGAATTAC	60	Rsa I	161 124, 37	235 236
C69T	187.5	24	CAGCGCTTCCGCGGCTCTTAG CCACTCACTCTCGTCCGAATTAC	60	BsmAI	345 310, 35	237 238
C127G	187.5	24	CTGGCTTTCTGCTGAGTGAC GATCAAAAGTCCCCGAAACC	60	co0109	284, 175 459	239 240
A(-362)G	187.5	24	ACTCAGTTGTATAACCCACTGAAAATGAGT TTCATAGATGTTATCATCTGGG	55	Mbo II	224, 26 134, 90, 26	241 242
A(-461)C	187.5	20	ACTCAGTTGTATAACCCACTGAAAATGAGT TTCTATAGATGTTATCATCTGGG	55	Hinf I	150, 100 123, 100, 27	243 244
G(-720)A	187.5	20	TCATCTAAGGCACGTTGTGG CCTCAAGCCTGGAGTGACTT	60	Hpa II	450 306, 144	245 246
G(-1027)A	187.5	20	ATGGCAAACAGTCTCCAAG ACCTAGCGCTGTGTCTCTG	60	Nco I	170, 41 105, 65, 41	247 248
A(-1095)G	187.5	20	ATGGCAAACAGTCTCCAAG ACCCTAGCGCTGTGTCTCTG	60	MspA1 I	211 172, 39	249 250
insCCCT(-1163)	187.5	20	TGTGTGTCCTCCCTTCCATT CTTGGAGGACTGTTGGCCAT	60	Mnl I	144, 28, 11, 4 100, 48, 28, 11, 4	251 252
insG319	200	27.5	CCCCTGCTGCTTTATCTTTCAGTTAATGACAGCCCGG ATCCCCAACTCAAAACCACA	55	Sma I	246 210, 37	253 254
G378C	200	27.5	GCCGCTGCCCTCCAGGGCTCCCGAGCCACACGCTGGG ATCCCCAACTCAAAACCACA	55	Acl I	108, 41, 33, 5 141, 41, 5	255 256

* Bold indicates mismatch in oligo to create restriction site

Figure 18

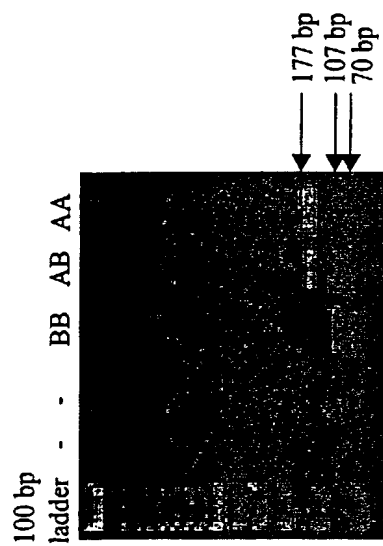


Figure 20

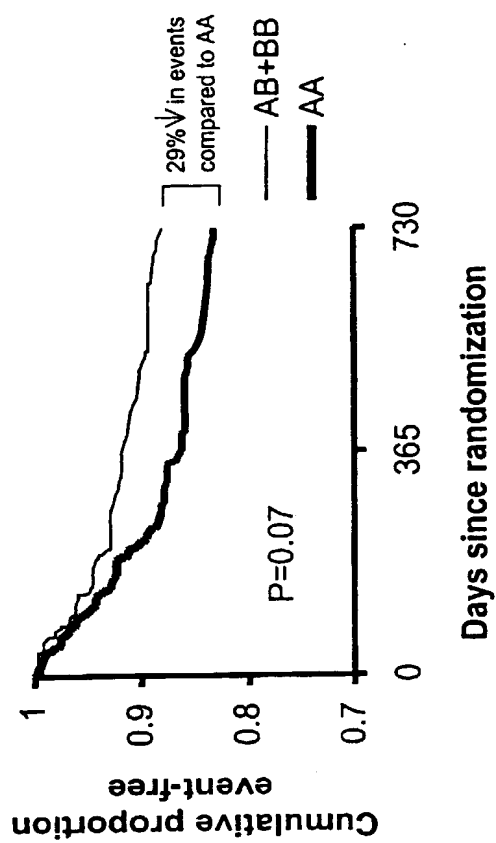
R219K	P-value			P-value			P-value		
	AA	AB	BB	AA vs. AB	AA vs. BB	AA vs. AB+BB	AA	AB	BB
n	424	330	36						
MSD	2.70±0.37	2.77±0.37	2.78±0.40	0.01	0.22	0.005			
MOD	1.73±0.35	1.81±0.35	1.85±0.35	0.002	0.05	0.001			
MI before trial %(n)	48.3 (205)	47.1 (155)	33.3 (12)	0.71	0.12	0.48			
events during trial %(n)	17 (71)	13 (41)	11 (4)	0.10	0.49	0.09			
total events ^a (%)	65.1 (276)	59.4 (196)	44.4 (16)	0.11	0.01 ^b	0.04 ^c			

^a Total events is calculated as the number of events/total number of individuals. Thus, the maximum value for this variable would be 200%, as individuals may have had events both before and during the trial.

^b Odds ratio for BB vs. AA=0.43, 95% confidence interval 0.22-0.85

^c Odds ratio for AB+BB vs. AA=0.74, 95% confidence interval 0.55-0.98

Figure 21



WO 01/15676

PCT/TR00/01492

Figure 23

	n	< median mean±SD	n	> median mean±SD	P-value < vs. >median	P-value AB+BB vs. AA < median	P-value AB+BB vs. AA > median
AB+BB							
Total Cholesterol	193	6.22±0.91	172	5.87±0.82	0.0001	0.22	0.43
HDL cholesterol	192	0.91±0.22	171	0.94±0.23	0.21	0.12	0.37
LDL Cholesterol	192	4.49±0.84	171	4.19±0.78	0.0005	0.03	0.57
Triglycerides	193	1.82±0.79	172	1.65±0.72	0.03	0.02	0.85
MSD	193	2.79±0.37	171	2.75±0.37	0.30	0.18	0.01
MOD	193	1.83±0.36	171	1.78±0.34	0.18	0.09	0.006
AA							
Total Cholesterol	207	6.11±0.86	217	5.94±0.84	0.04		
HDL cholesterol	206	0.88±0.20	214	0.96±0.24	0.0002		
LDL Cholesterol	205	4.32±0.77	214	4.23±0.72	0.22		
Triglycerides	206	2.02±0.82	217	1.67±0.67	<0.0001		
MSD	205	2.75±0.36	217	2.65±0.38	0.006		
MOD	205	1.77±0.34	217	1.69±0.35	0.04		

Figure 24

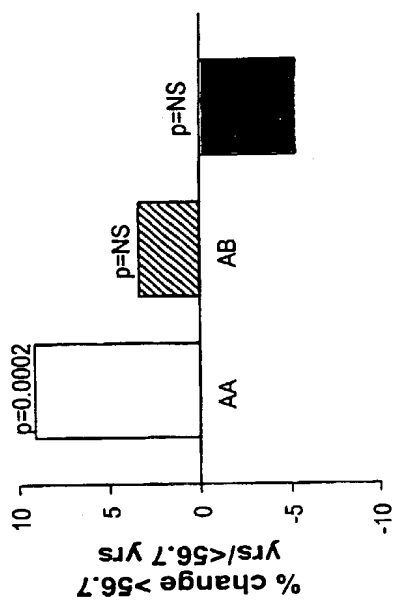


Figure 25A

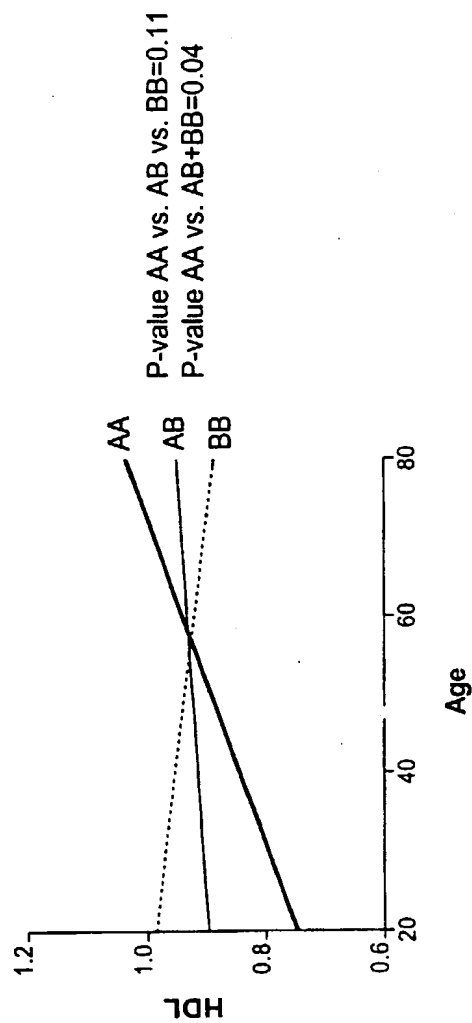


Figure 25B

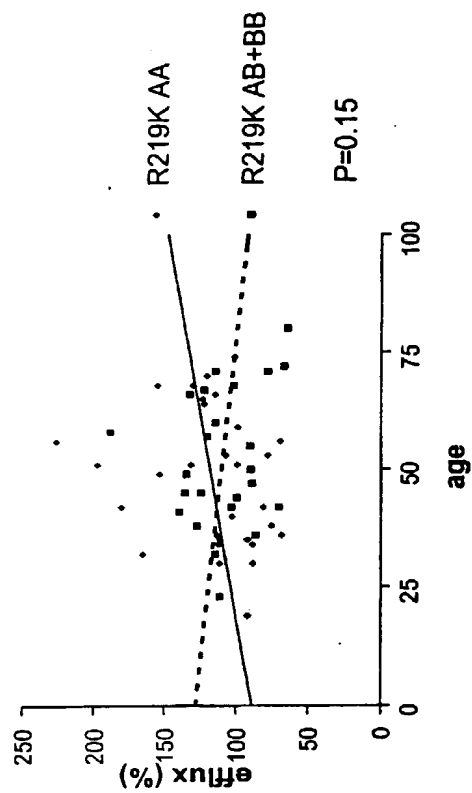


Figure 26A

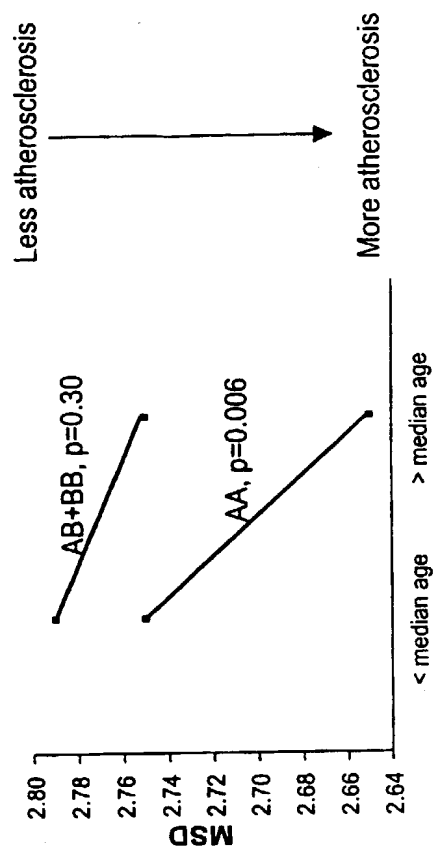


Figure 26A

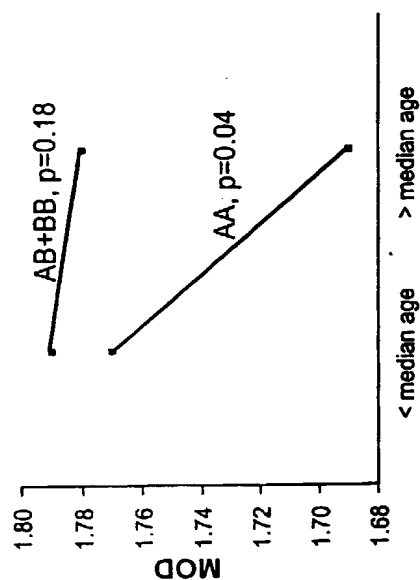


Figure 27

	South African Black ^a	Cantonese	Dutch ^b	P-value South African vs. Dutch	P-value Cantonese vs. Dutch
AA % (n)	1.3 (1)	32.7 (33)	52.5 (180)		
AB % (n)	50.7 (38)	55.4 (56)	45.2 (155)	<0.0001	<0.0001
BB % (n)	48.0 (36)	11.9 (12)	2.3 (8)		
n	75	101	343		
carrier freq.	98.67	67.33	47.52	<0.0001	0.0005
allele freq.	0.733	0.396	0.249	<0.0001	<0.0001

^a Not consistent with Hardy Weinberg equilibrium ($p=0.01$)^b Not consistent with Hardy-Weinberg equilibrium ($p<0.001$)

SEQUENCE LISTING

<110> University of British Columbia
Xenon Genetics Inc.

<120> Compositions and Methods for Modulating
HDL Cholesterol and Triglyceride Levels

<130> 50110/004WO2

<150> 60/151,977

<151> 1999-09-01

<150> 09/526,193

<151> 2000-03-15

<150> US 60/213,958

<151> 2000-06-23

<160> 256

<170> FastSEQ for Windows Version 4.0

<210> 1

<211> 183999

<212> DNA

<213> homo sapien

<220>

<221> variation

<222> (1)...(183999)

<223> N's are A,T,C,G, or other, including no
nucleotide. All K's are G or T. All Y's are C or
T. All M's are A or C. All S's are C or G. All
H's are A, C, or T. All B's are C,G, or T. All
R's are A or G.

<400> 1

```
gtctataatg gcatgccaca gggctctaaa actttgcagt tttatcatta actcaaatga 60
aatgtatata tgccgctgac tcaacatttt gagagacaac aaatacaatg aatatcaaga 120
tacatatata tataatatgt atttcttttt gagatggagt ttcactgttg ttgtccaggc 180
tgaggtacaa tagcacgacg ttggctcact gcaacctctg cctcccagggt tcaagcaatt 240
gtcctgcctc agcctcccaa gtagctagga ttacaggcat gtgccaccac acctgggctaa 300
ttttgtatatt tttaagtaga gatgggggtt caccatgttg gtcaggctgg tctcgaactc 360
ctgacctcag gtgatccacc tgcctcagca tctcaaagtg ctgggattac aggtgtgagc 420
caccaccacc ggccatatat atatattttt gagatggagt cttactctgt caccagggt 480
ggagtgaat ggcttgatct cggctcattg caacctctgc ctcccatgtt cagatgattc 540
tcctgcctca gcctctcaag aagctgggat tacagggtgca tgccaccatg cccaactaat 600
ttttatattt catcatgggg ttccaccatg ttggccaggg tggtgtcgaa ctctgacct 660
caagtgatct gcctgccttc ggcctcccaa agtgctggga ttaccggcat gaaccaatac 720
gcttggaat atttttttta gaaaaaaaaa ttccagggtg caacagcatc caaaaagtaa 780
ccaatgattt taggtgaagg gtgaagacaa atgtaaactc tttttttttt ttttgaaatg 840
```

gcgtcttgct	ctgtcgcccta	ggctggagtg	cattgggtgca	attgcgactc	actgcaacct	900
ccacctcctg	gactcaaacg	attctcctgc	ctcagcctcc	cgagtagctg	ggattatagg	960
ctcgcgccgc	cacgccccgc	taatttttgt	gttttttagta	gagacggggt	ttcaccatgt	1020
tggccaggct	ggtctcaaac	tcttgacttc	aagtgatccg	cctgccttgg	cctcccaaag	1080
tgctgggatt	acaggcttga	gccacccggt	gaaatgtaaa	ttgttaaacc	tgtgtttttg	1140
aaaatgcata	agtataggat	aaggggagaat	tgactttctg	aagaccagaa	catttttagtc	1200
aattttcaaac	acaatgtgag	tcaattgtat	aaaacagggt	ccttatcctg	atgaggataa	1260
gaatagtatc	cttggtcagat	ggaaatgccc	attcagctgt	actttctagt	ggttacgccc	1320
atagtagcac	tgttgatgga	accagggtatc	tgacttttagg	aaagatgttc	cccaactgga	1380
gctgacccag	aggagcctga	ccaacttggg	gaaagttaa	agatctcatc	acgtggagaa	1440
taggggaagg	caccaacacg	tattgagtggt	ctacttttag	cttaaggagg	aaggagaaaa	1500
ggcagggaa	aaacggagga	tggaaataaga	ataggtaatc	ttccttaggt	ttaaataata	1560
agtgtctgcc	ataggaagga	gccccagaac	acagttatca	ataatagaga	ctcacacaga	1620
gcattctaca	ctagagctgc	tgtcctcctg	accagaataa	gggtaagggtg	tgtgtgcgtg	1680
tccaggaaa	taggcagcta	ggaggtgatc	agagcatata	ctactgccgc	cacaattcta	1740
agtgtcttcc	cctaggggaa	tcctatttct	tctcaggcac	atttgtttat	tcattccatg	1800
ttcactcttg	ttattttactt	cttgccaggc	tttgtgttaa	gaattgggga	aacaagggtg	1860
aataaaacca	gtctgtaaa	aaaaggagct	cacagtctgg	aggggcaaat	gggcattgtg	1920
cctgcaagtt	ggcccaactga	gagcctaaga	agtgaagtta	tgaatccagg	attactcagt	1980
tatcaatgaa	gtgattaaac	atcatccata	cagaccttca	gagctggagg	gaattttgga	2040
tacctactca	gcacatagtt	ttcaaacagt	gccttgtgga	accctagggc	atttcttagg	2100
gattgtctgtg	tgtgagagag	gagattgaat	cagaagggtgt	ctgggaccat	tctctactca	2160
cacttcaagc	agagcagctc	cacttctatc	tgtattatta	tttttattat	ttatttattn	2220
tatttatttt	gagacggagt	ctcgccctgt	cgcccaggct	ggagtgcagt	ggcacgatct	2280
cagctcactg	caacctctgc	ctcccgggtt	caagagattc	tcctgcctca	gcctcctgag	2340
tagctggaat	tataggcccta	tgccaccacg	cccagcta	tttgtattt	ttagtagaga	2400
cgggggttca	ccatgttgggt	caggctgggtc	tcgaactcct	gaccttgtga	tcaccgggcc	2460
ttcgccctccc	aaagtgtctg	gattacaggc	attagccacc	atgccccgcc	tatctgtatt	2520
atttattcat	tattgtctatg	tgaatgaacc	tgaagaatgc	ttactgttac	tgctaaagtat	2580
ttaaccacac	cccatgccca	tgcaggatga	tagtgaatag	tggccaaaag	atactataat	2640
tagactcatg	taattaagga	atatttttgt	cttgtaacct	ttatgtgcct	ataaagacta	2700
tgaatctctat	ttatttcagt	atattattgga	ataccaaaata	agcaaatgac	ctatgtgcta	2760
aagattctaa	tattgtgcta	agatttttct	tcagatgttt	ggctttctca	aattccctga	2820
gggctagaac	tttgccctac	tcattttgtgt	ttcccaagtg	tctaaccgag	tgccctgacac	2880
atacaggatc	tcctaaacgct	tgtctaatgt	gtgaggaagg	aattaaaata	atgtaccgcc	2940
gggcaaaagt	gctcatgcct	ataatcccag	cacttttgaga	gaccgagggtg	ggcagatcac	3000
ttgaggtcag	gagctcgagc	ccagcctggc	caacatgggtg	aaaccccgct	tctactaaga	3060
atacaaaaat	tagccgcgag	ttgtggcagg	cgctgttaat	cccagctact	cggaaggctg	3120
aagtgggaga	atcacttgaa	cctgggaagc	agaggtcgta	gtgagccgag	atcagaccgc	3180
tgagctccag	cctgggtgac	agagcaagac	tccatctcga	aaaataaaaag	taaaataaaa	3240
taatgtacta	actggaccca	gaacagattt	tccaattgat	tattgacaac	aaaggaatct	3300
gaattatttta	ataaggtgaa	taagtacata	ttcatatata	tatgtatatt	tgtgtgtatt	3360
tacatttttta	taaaagtgtg	aaagtatata	tacttttttt	cctttcttca	ggtagaaaacc	3420
tctcctagat	tgtcactgaa	taaacattag	cactaactat	ggcaatcaaa	tcacatattg	3480
attggtgtca	gagaagaatt	gaacattcaa	ctctgaagca	gtgttatattc	ttccatctgc	3540
aaacactctg	tcctccatcc	httctttgtg	tatcctggaa	tccaagtcat	aaataatgat	3600
aggtattttct	gtcaaaaggta	tttctcagag	gagtgatatg	taactccctt	tcctctgata	3660
cactgactca	ctaagcagct	acccttgtga	attccaatta	gcaatacttc	ttgctatgtc	3720
tgggtccaact	ttcagacaaa	cctagtgttc	aggattcccta	tagccattta	taggtgtaga	3780
caggaagcat	tcagatatcc	ccagagggtac	ctgataacca	gctgatccat	gactgtctgt	3840
cttgggcttg	gccagcttga	aatcttgaca	ttgtggttct	cnccagaga	aggtgccttt	3900
tggatgtgag	ataaagacat	tatgactaga	tajtgcatgg	tgaggggtgtt	tttctagtgtt	3960
taccgaagtg	ttgatctgta	aagctgctac	cagcacacac	nnanncacac	acacacacac	4020
acacacacac	acaattaacc	acagatatcc	tcatgggaaa	ttgtcttagg	aaagaatgga	4080

agccaagatt	ttatatatag	accacagaag	gtgatgggta	atgttcttgg	aagggagttg	4140
acaggcaata	gctataagtt	aactcaggaa	agcaaagaaa	atcccccagg	agctaaggga	4200
gagggttagag	attctgcttt	ttattagcaa	ttcatagctc	tcaagtttca	tacagtcttt	4260
aaggctcccc	tcttcataata	gaataaatga	aattatttta	taaattgttc	ctcagattcg	4320
tatctgtaca	ttctgggacc	acgagttgta	gcaggatgtg	attttccctca	ttctgggcat	4380
ctaagttcta	cagttaagga	cactgaaaca	aacctttagt	cgaataaaga	ttggcaccatt	4440
gtttcttctc	ccataaacat	tgaatgggtcc	aggaagggcc	agggtgtggtg	gctcacacct	4500
gtaatcccgag	cactttggga	ggccaaggca	ggtagatcac	ccgaggtcag	gagttcaaga	4560
ccagcctggc	caagatgggtg	aaaccctgtc	tctactaaaa	atacaaaaag	gaggagtggg	4620
agtcccgagct	tttgcagtaa	tgtccacatt	gggactttat	cttaaatgtg	caagacacaa	4680
ctcttggcca	ggcgtgggtga	accgagattg	tgccactgca	ctccagccag	agaatgcact	4740
ccagcctgag	caacagagcc	agactccttc	tcagaaaaaa	aaaaaaaaaa	aaaaagacaa	4800
ctcttaaatct	ggtgttctac	tgtccttgaa	ccaccatacc	tttgcagaag	tcattctaga	4860
tcattcaatct	gaccataaaa	cacagtttgc	caaactggca	actaactgca	cctattttgtg	4920
attagtttgg	aagaaacttg	aaagtgcctc	ttttaactgt	ccacttattc	cctgcctggg	4980
cacggaattc	tctcccacgc	ttaataacgg	acacttttaa	aaattatttt	tactccccac	5040
agagttggca	gatttgcgtt	tcagagagtt	aaatggaaatg	cctccagttg	aagtatcccc	5100
ttttctagaa	tggaaagtct	atcttcacag	tgtcataatc	caggtgcctc	gggctgagac	5160
ttcccctggc	taggcgggtac	cctgggttagc	acagctgaac	tggctgtgaa	ctaaacattc	5220
atttttttatt	agcagccagg	ctggacagag	atcacacaag	accaacctga	caacagcagc	5280
atgctgctct	gcttcagaaag	taattttttt	tttttttgag	acaagagcct	tgctctatca	5340
cccaggcaaaa	gtgcagtggc	atgatctcgg	ctcactgcaa	cctccacctt	ctgggatcaa	5400
gcgatttctc	tgccctcagcc	tcccagtagc	ctgggattac	aggcgcagtc	caccatgcct	5460
ggctaatttt	ttgkactttt	gtattttttt	tttttttgag	atggagtccct	cgctctgtcg	5520
ccggggctgg	agtggcctga	gccaccgcac	ctggcccttc	agaagtaatt	tttaagggaag	5580
gatcttgtcc	tgggtggggg	gttgggcaag	gctgtgaaaa	gcaaacaaaa	atcacatgtg	5640
gcctaataagg	aggccagtgg	aaatacacat	gatgaaaaag	aaacttacaa	aagcacatta	5700
ttaattttctg	aacatgctaa	taccatccaa	taacaataag	atctaattatt	tattgaattg	5760
tgattactca	tcagctacat	tccaagtact	tctacatgta	cagttatgtg	acacataaga	5820
tgtttaggtc	accactgaca	gaatgtatga	tggtagcccc	ataagattac	aaaaattcct	5880
attgcctagt	gacatatgta	gcaagatgca	ttactcacgt	gtaataagta	atgtgatgct	5940
gctgtaaaaca	aacctactgt	gctgccatgc	ctatagaagt	ctaggacggg	ctgggcacag	6000
tggctcatgc	ctgtaatccc	agtacggtgg	gaggccaagg	caggccgatt	gcttgagccc	6060
agaagttcaa	gaccagccgg	ggcaacatag	tgagagcctg	tctctacaaa	aaatacaaga	6120
acaaattagc	caggcatggg	ggcgcatgcc	tttgggtccc	gctactcagg	aggctgaggg	6180
aggaggatca	cttaagccca	ggaggttgag	tctgcagtga	gccatgatgg	tgccactgca	6240
ctccaacctg	gagagagagt	gagaccgggt	tttaaaaaaa	aaaaaaaagg	taacaaataa	6300
aagtatgtat	agtacagaat	acttggtaat	gataaaacagt	atgttactgg	tttatgtgtt	6360
tactatactt	tttatttttt	agagtatact	cctacttatt	taaaaagaaa	aaagaaagtt	6420
aactgtaaaa	caggcttaga	caggctccttc	aggaggtatt	ccagaagaaa	ggcattgtta	6480
tcacaggaga	tgaaagctcc	atgcatgtta	ctgcccttga	agaccttcca	gtgggacaag	6540
atgtgaggtg	gaagtctatg	atagtgtatga	tcctgacctt	gtgtaggcct	aggctaatat	6600
gtgtgttttt	aacatattag	tttttaacaa	caaagttaa	tcagttaaaa	caattttttt	6660
aatagaaaaa	agctcataga	ataaggatat	naaagaaang	acaatgtttt	gtttgtttgt	6720
ttgtttgttt	tttgagacag	agtctcgctn	ccatcacctg	ggctggagtg	cagtggcaca	6780
atcttggctc	agtgcacact	ctgattccca	ggttcaagta	attctcatgc	ctcaacctcc	6840
caagtagctg	ggattacagg	cgcccatcac	cacaccaaac	taacttttgt	cttttttagta	6900
gagatggggg	ttcatcatat	tggccaggct	tgtcttgaac	tcctgacctc	agggtgatcca	6960
ccctcctcgg	cctcccaaag	tgctgggatt	acgggttga	gccatcgtgc	ccggccagaa	7020
agaaaaatgt	tgtacagtat	gtacgatgta	tttgttttaa	gctaagtgtt	attatgaatg	7080
aatcatgtgt	gggtagtggtg	ctcatgcccg	taatcgcatc	actttgggag	accgaggacg	7140
gaggatagct	tgagtccaga	gttctagacc	agcctgaaca	acgtgggtgag	acctcgtctc	7200
tacgaaaaatc	atcaaaaatt	atccatgcgt	gggggtacat	acctatagtc	ctagctactc	7260
aggagactga	ggtgagggga	ttgcttgaac	tcaagaagtt	gaagctgcag	tgagctataa	7320

ttgtaccact	gcatttccggc	ctaggtgacc	ccgcctcaaa	gaataataat	aaaagctggg	7380
cacggtggct	cacgcctgta	atcccagcac	tttgggaggg	caaggcgggc	ggatcacttg	7440
aggtcaggag	tttgagacca	gcctggctga	catggtgaga	ccccgtcgct	actaaatata	7500
aaaaattagc	cggtcgtggg	gggtgtgtgc	tgtaatccca	gctactcagg	aagctgaggt	7560
gggagaattg	cttgaacctg	ggaggcagag	gttgcaagtga	gccgagatag	cgccactgca	7620
ctccagcctg	agcaaaaaac	aataataaat	aaataagttt	gaaaatttaa	aatgtttata	7680
aaattaaaaa	gttacagtga	gctaagattt	agtattaaag	aattttttta	taaacatgta	7740
gtgtaactct	acagtgttaa	taaactctac	agtagtgtac	agtgacatcc	taggccttca	7800
cattcactca	tactcactg	actcaccag	agcaacttcc	agtcctgaaa	gctccattca	7860
tggttaagttt	cctatacagg	cggtgccattt	aaaaaatctt	ttaggccagg	cgcgccggct	7920
cacgntctgta	atcccagcac	tttgggaggg	tgaggcaggc	ggatcacgag	ctcaggagat	7980
cgagaccatc	ctggctaaca	cggtgaaacc	ccgtctctac	taaaaatata	aaagatttag	8040
tggtgtgggt	gggtgggcgc	tgtagtccca	gctactcggg	aggctgaggg	aggagaatgg	8100
catgaaccca	ggaggcggag	cttgacagtg	agctgagatg	acaccactgc	gctccagcct	8160
gggccacaga	gcaagactcc	atctcaaaaa	aaaaaaaat	cttttatact	atattcttaa	8220
tgtacctttt	ctatgtttag	atacacaat	accactgtat	tacaattgcc	tactgtattc	8280
agtacagtaa	catgctatat	ggttacgtag	cctagggaaca	ataggctata	ttgttcctag	8340
gtatagggat	gtggtatcct	ataccatcta	ggtttgtgta	agtttatttt	atgatgtttg	8400
catgacgaca	gagtcaccta	aggactcatt	tcttagaata	tattttagt	taagcaatgc	8460
atgactctat	tgactcatga	attcttacca	cagacctatg	gggcagtact	attgttacct	8520
tcattttata	aatgataaaa	ctgagggtaca	gagacagtaa	ataacttgac	cacggtcatt	8580
cagctactca	agagtcaagg	ctgggattta	aaaccagatc	acatggtttc	agagtgttca	8640
cacttaccta	ctatactgtc	tcaagagcaa	ggatgttttg	gttcacttga	caaatagaaga	8700
tagggacctc	tttcattata	agcctatttt	aggctaaaaat	agaagggaag	gggacacagt	8760
gaatccaggc	cttctggcat	ggctcctcag	ccctttctga	gctggcctgg	gacagccttc	8820
ctacctcact	gatgccactt	cctactgagc	gactttcctg	cctacctcac	tgatgccact	8880
tcctactgag	cgactttcct	gggtccaga	cccagtaagc	gactttgcct	gcacccacct	8940
tattttgctc	tactccctgt	gcttttatgc	ctttaccat	ctgccctgga	aagctcttct	9000
aacctttgaa	tggttaaagg	cataaatgta	tgctggagaa	atcctcagct	cagggccagg	9060
cacgctggct	cacgcctgta	atcccagcac	tttgggaggg	cgagggtggg	agatcacctg	9120
aggtcgggag	ttggagacca	gcctgaccaa	catggagaaa	ccctgtctc	tactaaaaat	9180
acaaaattag	ctgggcgtga	tggcacatgc	ctgtaatccc	acagctactc	gggaggtcta	9240
ggcaggagaa	ttgcttgaac	ctgggagggc	gaggttgacg	tgagccaaga	ttgcctctct	9300
gcactccagc	ctgggcgaca	gagctagact	ctgcctcaaa	aaaaaaaaac	aaaaaaaaaga	9360
aaaaaaagaa	aaaaaaagaa	tcctcagctg	agttgtcaac	tcctctttga	aactttctca	9420
gacctttcag	gctgagtcgt	cgctcatttg	tgcttctctca	gttctctggct	tctaccttct	9480
tcatagcttg	tttcatgtaa	tgtaaattct	tacttgcttt	ctccctcttc	taagctgaga	9540
gctacttcaa	agcatgggta	ggacctagca	cggtgtatgg	gacatgggtg	gtaccccgta	9600
aatgtttact	gaaaaaaaaa	tgcttaaagc	aattgttaac	atcatcagat	agataattat	9660
gggcattcag	agattctgtc	ttcaagctta	tataaagaac	ttatttttgg	ctctaattat	9720
cctgataatt	ttctcattac	tttcacttat	tggtgcttgt	ggatcaattg	ttgacatttt	9780
ataaacattt	cactatttga	caatgatgat	actaaaatac	gaattaagca	accattctaa	9840
agatagtgat	gatgataaca	tatacgctgg	taacatcttt	attttcagcc	gtatcatgga	9900
atcctctgtt	tccattctgc	taggtaggca	ggtatgcagg	tagaacttgt	gagaggatat	9960
gatttttgtt	tccatcttag	atatgacagg	aacttggaat	ttttgacata	aatgacgaac	10020
atccgggatt	cttaacaat	ctttaaaaat	ggaatgcctt	aaaagctggg	cgcagtggct	10080
cacgcttata	atcccagcac	tttgggaggg	tgaggcaaat	ggatcacttg	agttcaggag	10140
ttcaagacca	gcctggccaa	catggtgaaa	ccccatctct	actacaaata	caaataattag	10200
ccgggcgtag	tggcaggcgc	ctgtaatccc	agctacttgg	gagcctgagg	caggggaatt	10260
gcttgaaccc	aggaggcctt	ggagattgca	gtgagctgag	actgcgccat	tgcaactccag	10320
cctggggcaac	aagagtgaac	ctccatctcc	ggaaaaaaa	aaaaaaaaaa	aaggaattgcc	10380
tttgggaata	atttatttat	aatttatgta	taacatatag	acaaaccatt	agttgtctct	10440
atattttact	aaatataaat	ttagtataat	taaatattta	ctaaatataa	aaactcttag	10500
attttactaa	agagttacaa	ctaattggcc	tggtcggtg	gctcacacct	gtaatccag	10560

cacttttagga	ggcagaggtg	ggccgatcac	gaggtcagga	gatcaagacc	atcctgggcta	10620
acacgggtgaa	actctgtctc	tactaaaaaa	aaaaaaatac	aaaaaattag	ccgggctgtg	10680
tggcaggccc	ctgtagtccc	agctactcag	gaggctgagg	caggagaatg	gcgtgaacta	10740
agcagaggct	tcctaaaaag	tgatcttcag	gataaaaggca	gaggaagagg	ctccatgact	10800
gggatttggtg	ttgaggagag	ccagagaagc	aagctacaga	aaagagaaaa	aattaatatg	10860
caagagagta	aaacaacacga	aggaaaagaa	cccagtgtgg	aaacactaca	cgtgagaaag	10920
gtgtctgtaa	ggatgtttcta	caaagcaaat	gcttggatat	taattcattg	cagcaggaga	10980
tggttaagcct	catgataaaag	aaggagaaaa	aatcaagtca	agggctctga	ggtactgacc	11040
caggtatact	tgactatgcc	agcaactggt	tagggggaga	tttgagctac	acttgttagca	11100
aaggcaaaaat	ctgtaattag	ttgtaactct	tttttttttt	gagatggtgt	ctcgtctgtg	11160
ccccaggct	ggagtgcagt	ggtgtgatct	tggtcactg	caagctccgc	ctcctgggtt	11220
caagtgattc	tccagcctca	gcctcccaag	taattgggac	tacaggcatg	caccaccatg	11280
cccagctaatt	ttttgtactt	ttattacaga	ccatgttttg	ccatgttcac	caagctgggtc	11340
tcaagctcct	gacctcaagt	gacccgtccg	cctcggccnt	cccaaagcgc	tgagattata	11400
ggcctgaacc	accgcgcctg	gcctaaagag	atctaattct	tagcaaaagt	tcaccaggga	11460
gtctctctc	acccccaccc	catccttccc	acaaagaatt	agaacaatgt	ccctactacc	11520
cctgctgtat	ctctgacttt	ttacttttaa	tctcagcaga	atattttact	aaatgttttg	11580
atgtggttat	ataaaatcat	ccctgctgac	aaggaaacac	tttttgaaaa	aagttttcat	11640
tatcaaacac	taagtacagc	tgactgccgt	gacctttaac	ccatttctga	gtctccctc	11700
attggacttg	ggtggagggg	actggtagca	ataaaagtcaa	atgcttaata	atztatgcaa	11760
gtgcttgaag	aaatttgaag	ttgaatat	ctatcatctt	gaaatggaga	aagaatctgt	11820
aaacagcaaa	gccagacgcc	ctaaaggaaa	agattttacag	attaaaaata	gattgcaatc	11880
tggtaaaaat	atgtgcaaca	catgtaacag	tcagaaagtt	gaaacacttg	gtttaacawg	11940
agcttttawc	agataaaata	ggaaagaata	aacattggat	tttaaacacc	gataaacatg	12000
aaaagatgtt	taatctttat	ttttatttta	tccatattat	ttttcagttt	aatcaaaagaa	12060
aataataaat	aaaacaataa	tacattttat	atataatat	atataatat	atataatat	12120
atataatat	taggcataag	ttaaagactg	ataagactgt	tgaaaaaggga	tgaaaaacta	12180
ggcttactca	taccaatata	tatctattag	gatgggctaaa	gtaaaaaata	ctgaaaaat	12240
caagtctcca	aaaggatatg	gagcaattgg	aacctctcaga	catcgctgrt	ngagaaaaca	12300
aaatggtaca	gccaccctgg	agaacagttt	agctgtttct	tgtaaagtta	aacatgcgct	12360
taccatataga	ctcagcaatc	tcactcctgg	gtattttatgc	taggaaaagg	aaaatttata	12420
cttgcacaca	aaaaacttgt	aagtgaatct	ttatagcagc	tctattcata	actgccaaaa	12480
actgagagaa	aatgtccttt	aatgtgtgaa	tgataaaacc	aactgtgcaa	catccatgta	12540
atgaaataact	acttagcaat	aataataata	atattaaaaa	cccagaacc	attgatgcac	12600
gcaacaaata	tggataaatc	tcaaaagcat	tatgctgagt	aaaagaagtc	agtctgaagg	12660
atttcatact	ctaggattcc	atztatataa	cattatttgaa	acgacaaaat	tatggggaca	12720
gagaatagat	cagcggttgc	caggggttta	ggtgtgtgga	gaggggtgtg	ctataaagaa	12780
catgcaaggg	aatttttttg	ggagatgaaa	tggaatctgta	tcctaattat	ggtcatggta	12840
acacaaatct	atacatgtgt	ttagattcat	agaactgtat	accaaagaa	aaaaagtcac	12900
ttttactctc	ttaaaaatgaa	aaaagaaaaa	gcctgggcat	tctaacacct	tgtttgtgag	12960
agtacacatt	gataccaagt	tttatgggtg	gcaattttgc	tataaatacg	gaaagtttgt	13020
ctgttctatt	attcagcaat	cccagttttg	caaaactatg	ctaaagaatc	tttgggggccc	13080
gggcacgggtg	gttcacgcct	gtaatctcag	cactttggga	ggccgaggtg	gacgatcacc	13140
tgaggtcagg	agtttgagac	cagcctggcc	aacattgggc	aacctgtct	ctactgaaaa	13200
tacaaaaatt	agccgggcat	ggtggcgcat	gcctgtagtc	cgagctactc	gggaggctga	13260
ggcaggagaa	tcacttgaac	ctgggaggca	gaggtttag	tgaactgaga	tcgtgccacc	13320
gcactccagc	ctgggcaaca	gagtgagaat	ccgtctcaaa	aaaaaaaaaa	aaaaaaaaaa	13380
caaaacaaaa	caaaaaactt	tgtgtacgtg	tgcaaagaga	atacaaagat	gatcatggct	13440
gcatttttta	aatgactata	aaaaagaggt	acaaccagcc	aggtaaagtg	gtgtgcacct	13500
gtagtcccag	ctactcggga	gggtgaggtg	agaggaacac	ttgagtccag	gagtttcagg	13560
ccagcctggg	caacatagtg	agaccctgt	cccaaaaaa	aaacaaaaa	ccaaaatgtc	13620
tatctgtagg	aatttgtttt	caagtgtgta	tacataggta	cagtgaata	ttatacatte	13680
atttaaaatg	atgataaaat	ctgtatttgt	ttacatgaaa	aactgtccac	tataatgtag	13740
tgaaaaataat	agattacaaa	caatatatat	ggaataaaact	tgtttagaaa	caatttctag	13800

```

aagaaggtag aatggacaga attatctctg ggaagtgggt ttataatgat tctcattttc 13860
ttcttttgat cttttttcata gtctttctac ttttggtatg tctggacatt tgattatgag 13920
catgtattac tgatctatct taaaaattga ttttaatttt tacaaaaact catgtaaaagc 13980
ttgaagggtc gcatttttaga ccatgtttaa attttctctg atcaaaacag acttattcaa 14040
atatcttgta ccctgtcctc caaaattgcc tgccaaaata cactacaaaa gagagcattt 14100
agctgcata tttttggact gctgagatca acaatattat ttaccatggc ttaaaatttt 14160
acctccagat atgtgtgggt tacaaacact cttccacatt tttgaggcat tgcttttgat 14220
atttttaagt taaattcagc tgtgcgcggg ggctaacgcc tataatccca gcactttggg 14280
acgctgagga aaggatcact tgaggtcagg agtttgagac cagtttagct aacgtgggtga 14340
aaccctgtct ctttttaaac tacaaaaatt aaccgggcat ggtggcaggc acctgtaatc 14400
ccagctactc aggaggctga ggcaggagaa tcacttgaac ttgggagaca gaggttgtag 14460
tgagccgaga tcatgccact gccctccagc ctggccacag agcgacactc catctcaaaa 14520
aaaaaaaaaa aaaaaaaaaa aaaggccagg cgcagtgggt cacgcctgta atcccgagc 14580
tttkggagcg ccaagggtggs sggatcaact gaggttgagg gttcacgacc agcctgacca 14640
acatgcagaa acccygtctc tactaaaaat acaaaattag ccgggtgtgg tggtacatgc 14700
ctgtaatccc agctactcgg gaggtctagg caggagaatt gcttgaaccc aggaggtgaa 14760
ggttggtgtg agctgagatc ccgccattgc actccagcct gggcaacgag caaaactctg 14820
tctcaaaaaa accgaaaaaa ttcccccaa aaacaaaaaa aaaacagcaa caacaaaaaa 14880
atcaaatat gtaccttggt tagcataaag cataattata tgcataatgg gattgggagg 14940
atgaaatgga aagggtatct attactgact tcagaaatta tgcctgata gattgatggg 15000
tgatttaaat ataacttctt gtcaagcatc tgtttttaga atcaaatatc tatgactctg 15060
cagtttctct gaaatctcat agtatcacat ctctgtttgc ctttgcattg ttttaagaaa 15120
atgaggatgt tgaaacttca aacttcggtt tcattgtatt acatttttga atgacacact 15180
ggtcatttcc tagaaatata aggtgacaaa tatttcacag aaacataagg tgctattatc 15240
tcattcaatc ttaggtcact caaaactctt tctctccac acattgaaga ttcatttggg 15300
aatgcttttg tcttattgtg caccctcagc gaagggtgg taagtgtttt tcattttgct 15360
tcttttggtt atctacaggg ttccattcaa taaacaaagg gacttgggtc aaacttcagg 15420
ctcttatggg tttggatgta atctttggc tcatttttag ttaccaacag agagtgttgc 15480
ttctgacctc tttgactctt ccctgctgaa tttactatgc ctttgatact tgtgaagggt 15540
gagattttcg aggagtactg ttgtttttgt tagaggtgtt aatgtctttc ttcgctttgt 15600
gattcaagtt gtgttcagtt acaatcataa gcattgtgct aaaaaaatca gatgcaaaact 15660
agcaaaaagta gaaactcagg gtgacagtct ttaagaaaag atgcaattct tggggctggg 15720
tgcggtggct tatgcctata atcccagcat ttggggaggc caagggtggc agatcgcccg 15780
agggtcaggag ttcgagacca gcctggccaa tgtgttgaaa ccctgtctct actaaaaata 15840
caaaaatttag ctgggcgtgc tgggtgggtgc ctgtaatccc agctactcag gaggtctagg 15900
caggagaatt gctggaacct gggagggtgga ggttgcagtg agcctagatt gcgccattgc 15960
actccagcct gggcaacaag agcgaaactc tgtctcaaaa aaaaaaaaaa aaaaaaagat 16020
gcaactctta ttactgacac agaaaatgaaa atttagttac atagtattgt aaaaggacta 16080
tcagctaggt ttagccttac caagatttag gtaattcatt tctgtctaca ctcatattct 16140
cagccacttc cctcatcaca ttttcagggt gcagtatata atagcgtcaa ctctgtaat 16200
tccccctact ccccatgaac ttctaggcca agggggccaca cgggttgagg catatagtat 16260
aaaggagtaa ggcagactgt tggagaaaaa cagggttagt gccaggtgag gtggctcacg 16320
tgtgtaatcc cagcacttta ggaggctgag gcgggcggat cagcaggtca agagtttgag 16380
accaggctga ccaacatggt gaaacctgt ctgtattaaa aatacaaaaa ttagctgggc 16440
acggtggcag gcgcctgtaa tcccagctac tcaggaggct gaggcaggag aattgcttga 16500
acctaggagg cggcggttgc agtgagccaa gatcacacca ctgcaactca gcctgggtga 16560
cagagtgaga ctctgtgtca aaaacaaaaa taatacaaaa aacaaaaaca aaaaaaaa 16620
aaaaacaaaa acaaggatta gtgaggactt tgcaaaagtgc aaacagcatg ctccatctaa 16680
agagagcttt tcagtactag ctgattgttg ttgtgtggaa atacgtcttg tatggtgaga 16740
tcttccacct tttcaacaga aatgagaaac acaaacattt ctgtgtgaca cttccaaact 16800
tgttggctat ttctgttttt ctttttttct cttttttttt tttgaggcag 16860
agttttgtct tcgttgccca ggctggagtg caatgacgtg atcttggctc gccgcaacct 16920
ctgcctctct gattcaagcg attctcctgc ctcagcctcc caagtagctg agacatgtgc 16980
cgccatgcct gactcatttt gtatttttag tagagacggg gtttctccat gttggtcagg 17040

```

ctgggtctcga	actcctgacc	tcaggtgatc	catctgccta	ggcctctcaa	agtgcagggg	17100
ttatgggtgt	gagccactgc	gcccggccct	agttgggttat	ttcaaacaaa	atactaaccac	17160
tcttcagccc	aaaccatgtg	tcagagagct	gggtgtggcc	agtgggcccc	tggtgtgcaa	17220
ctagtcttca	gtgatgctac	tgtatgctag	tgacagcaca	actgaccact	gaaaatatgg	17280
tgcacgatgg	tgaacagatt	ggatttcccg	tatctctaga	accccagggc	tttgangggca	17340
attctgatag	atggaggggg	agcgaganga	gagaaagagg	agggagaggt	atcacatgaa	17400
agagatactg	gactttctgc	taataaatgg	gtgggtatct	gggtgagtag	ataggaaatt	17460
aaaaagaaat	atgagagatg	ggcgtgggtg	cttgtgcctg	taatcccagt	gacttggggag	17520
gctgaggtgg	gagtattggt	tgagaccagg	agtttgagat	cagtctgggc	agcatagtga	17580
gaccccgctc	ctaaacataa	aattttaaaa	aatcagncta	agcgtgggtg	tgctgtcctg	17640
taatcccagc	tacttaggag	gctgaggcag	gaggatccct	tgagcccagg	agttagangg	17700
ctgcagttag	ctatgattgt	gccattttac	actagcctgg	gtgagaaagc	aagactccca	17760
catctgagac	agagagagag	gagagaggca	gaccatattt	gaactccagg	ctggtgaata	17820
attcatactg	attaatttaa	ttgaaaatat	tattttaaaa	tttgagatgc	ggagttttgg	17880
aaagggttaca	tttattaaat	tattgttggg	ctatgaggaa	cacattgttg	cttgggaataa	17940
tatttaatta	tgatgatgat	gatgatgata	ataaatgaca	ataataaaca	actatcattt	18000
attgagcaca	taccatatac	caggcccagt	accaagcagt	tcacatatat	tatacatcta	18060
atacccgag	caactctata	aggcagctct	atattgttgc	tccatttgaa	agatgaataa	18120
actgaggtac	agagatgtga	agtaacatgy	tgatggacac	ccagatatka	tytkcagata	18180
agaaggataa	gtcagaagat	cagataagca	gaaagggttm	macacacagg	actytcattt	18240
agtagtaaac	tyttatgatt	ggctctaaaat	tctattttct	tttacagttt	acctactcat	18300
caaactctgtc	ttaactattt	ttgtctctcc	aaattctctt	ctgttctttk	ktactatgta	18360
cacatgcttt	taaaatatgt	taggatttgc	tgtttccatg	tgktaatttc	ttgtttgcct	18420
ttcttcattt	ataaactctt	tcctcctact	aattattgac	aaactctatt	ttcttttttt	18480
tttttgaaaa	actctatttt	tcataatcatt	tttctaaatt	taaaaatagc	atataaggct	18540
gggcatgggt	gtccacacct	gtaatcccag	cactttggga	ggctgaggcg	ggtggatcac	18600
ctgaggttgg	gagtttgaga	ccagcctggc	caacatgggtg	aaaccctgtc	tcaactaaaa	18660
ttacaaaaaa	aaaaagttag	ccgggcattg	tgatgggcac	ctgtagtccc	agctactcag	18720
gagattgagg	caggagaatc	gcttgaaccc	gggaggtgga	ggttgacagt	agccgagatg	18780
gggccactgc	attccaacct	gggcaacaga	gtgagaccct	gtctcaaaaa	ataaagtata	18840
tatatatata	tatatataaa	tattttacgtg	tgtgtgtgtg	tgtgtgtgtg	tgtgtgtgta	18900
tacatatata	tagcatgtgt	ttattttata	taattttgta	aatacagaca	tatatgaaaa	18960
aattacctat	aatcttacca	tcacacaggtg	attgtctgta	gcacctatct	gggatttttt	19020
ttttcttttt	tctttttctt	tttttttttt	tttgagctct	tttctaggca	catatatattca	19080
atgaaaaagg	ttatcaatat	agtaaacagtt	attttttatt	gaatgttaac	catcacacata	19140
aatatagctt	tgtctttttt	ttcaattcgc	atttaccatg	agcagtttct	ctatatcaca	19200
actctttgaa	aacattattt	tcacctttca	tggttatata	acattctatc	atgtgaattt	19260
atcaatgtgt	atttttagaat	tgttatccaa	tgattaagca	tttttaaaat	gttcactcat	19320
caataaaaata	gtgacaacat	tcttgaaacat	aagttttttt	taccatacta	tcggatattt	19380
ccttagtata	aattcctcca	agtaaaaatta	gtgggccaaa	ggcttttttt	ttttgaggcg	19440
gagtttcogt	ctcgttgccc	aggctggagt	gcaatgggtg	gatctcgggt	caccacaacc	19500
tcctcctccc	aggttcaagc	aattctcctg	cctcagccctc	ctgagtagct	gggattacag	19560
gcatgcacta	ccatgcctgg	ctaattttgt	agtttttagta	gagacagggg	ttctccatgt	19620
tggtcaggct	ggtctcaaac	tcttgacctc	agtgatctcg	catgcctcgg	cctcccaaaag	19680
tgctgggatt	acaggcatga	gccactgggtc	ctggaccaaa	gcctcttgat	acatttttgc	19740
aaactatcag	aatgttgggc	ctctttgcac	cctactaaca	ccctcagttt	ttatgagtat	19800
gattacatta	ttttccctct	tttccccaac	ctcctattct	attttcctta	gataccttaa	19860
gactgcaccc	ccaacttagc	tttctgttct	cattcaggca	gtgtgtccag	ggcttccaat	19920
cccagtggtg	agtaggcaga	tgtgggggct	tctgttgtaa	ctctgttagg	taattgagcc	19980
actcaagggg	aaaccagctt	tgggggtccgc	tctgtggcaa	gcccaggact	ctatngaagt	20040
gagctcattc	ctcactaatt	tacacaccag	gacaagtagc	cangctaaga	aattgtctta	20100
atttcactgg	tcgtcagtca	acaaaagaat	gaagatacag	aaggaaaata	aaaggcctgc	20160
tcccacagtg	gggtcatagc	acatctccac	atttaacctt	tgacaaggca	aaagtatttc	20220
ttctgtccag	acaattccag	aagtcataag	gaatactggg	caaggatggg	tcaaaacaac	20280

acagactatt	gagggcaaca	aaggaaaaac	catgcactcc	tgaagaaata	gatcccaaaa	20340
tgctgaacga	gaaagaggat	tgtctctcta	gaagtctaata	agaaaacagt	atctggaaca	20400
ttaaactag	gatttttttt	ttttctaatg	acttactctc	ttattaatat	gtcagagaaa	20460
agaatagctc	ctggctaaga	aatacaacag	tccctcatcc	cagaaatcac	agccaggaa	20520
atggattctt	aagtgtcaaa	aaagtactct	gaataaggaa	agaaacgcag	atgcactact	20580
tctattataa	taagcgcttg	atttctttta	atcccctgag	tccaattatt	ttcttggcaa	20640
atttaagggg	actgactgct	tctgtgaatc	tattgtttaca	cttgataatg	gatctgagtt	20700
gggggtaata	tttgccctatc	aattttggata	cttaaaaaatc	tctctctctt	tcttcatata	20760
ccctctatct	cacaactttc	catttaaatga	gggaagtga	tttctttttt	ctgcccctct	20820
ttcctactgc	ttctagaata	aaagcataac	aggacgacag	gagtggagat	gagaggaagc	20880
atttccaagc	aatgggaaag	tatgatgaga	gtcgtgagtt	ggtagaatgg	gggtgagtaa	20940
gggggtgggg	gtggatggat	ggaagaggat	ggaggaggaa	gcaggtcata	tgatcaggct	21000
tcaaaggcct	tccaatatct	tgttttcaga	ggctttgtag	gtcttcttac	agaactttga	21060
gtgtattttt	ctttgtgag	caaaggagaa	ccatagtaaa	ttttgagga	tgggctgggc	21120
gcgggtggctc	acgcctgtaa	tcccagcact	gtggcaggca	gaggcagggtg	gatcatttga	21180
ggtcaggagt	tcgagaccag	cctggccaaa	atggtgaaac	cccgtctcta	ctgaaaaaac	21240
aaaaagttag	ttggatgtgg	ttgcatgtgc	ctataactcc	agctactcgg	gcagctgagg	21300
cagcagactt	gctggaaccc	gggaggcaga	tgttgcaatg	agttgagatt	gtgccactgc	21360
actccagctt	gggagacaga	gtgagactcc	atctcaaaaa	aaaagaaatt	tttttttttg	21420
gagggagaaa	atatatgatt	agattgtttt	tgtgttggtt	tgcttgtttg	ttttttttcc	21480
caagcaaaaa	atcactttac	tgcaataggg	aagacaaata	ggaaggggaa	gaaactagag	21540
acaggaacag	cagtttgagg	gttctgcaat	acagaagccc	agatgtttgg	cttggaactta	21600
gacactggga	atgaaaaata	aatgatgaat	taaaaaaata	aaatatttgg	gaggtatact	21660
tgacctgacc	ttgggtgctt	ttcaaatgag	aagagaaaaga	tagagacaga	tgaaaaagtt	21720
aagcaaggat	gactatgatt	tcccatagtg	aatgtctgga	tgatgatata	attaaatgaa	21780
aattttttaa	aaggcagatg	gtagaaggag	atttgaagg	aagacaagaa	atttgtttgt	21840
tttggaattta	cttgtagaat	gacctgcaaa	attttgtcct	aataaatgtt	aacaagtggc	21900
tttccataca	aaaaccaaac	caaacaaaac	cctgatgtaa	accaaata	aaattctgag	21960
gcccccttc	accatctgaa	tgaacttctc	cctctgcaag	ggcactctta	aaatttaaca	22020
tgaaagactg	gttcagggtca	tgacgggaag	tgggggtcgg	acaggcctca	ttatgcctct	22080
ctggcattaa	catcaacaca	gaccttaagt	ctgttaagaa	gcatttacaa	tctattctct	22140
ctgaagcctg	ctacctgaag	gcttctctctg	cacactgaga	actttggtct	ccacaatcct	22200
ttatcttaag	ccagacattt	cctttctatt	gtcccagggt	ctttagataa	actcaaccaa	22260
ttgtcaacca	gaaaaatttt	aaatctatct	ataacctaga	agccccact	tcaagttgcc	22320
ctgccttttt	gaactgaacc	aatgtatttc	ttaaacttat	ttgattgaag	tctcatatct	22380
ccctaaaaac	caagctgcac	cccaaccacc	ttgggtgcat	gttcttagga	tctcctgagg	22440
gctgtctctc	gagggccaag	atcactcata	tttggtctac	cataaatctc	taaatatttt	22500
acagagtttt	actcttttca	tcgacactga	tttatattgg	atttccaatg	gtgtaattatt	22560
catgccgttg	gccgatttca	agctagctgg	tagagatatg	caaacaaaca	aacaaacaaa	22620
aagagatatg	caaaaaacaac	tcttgtgagc	ttgtgtgctg	gctccaacac	accatgctgc	22680
tggatattct	accaggcagc	atagggcgca	cggtgggtga	gcctggcaag	gagacaagag	22740
ctggaggtac	agggtttaa	tgaagccaag	ggcgtgaata	atattgatga	ggagagcaag	22800
tagaaatgaa	aagagaaaac	cagtattagg	agatctataa	agaaacaata	gtcagaaaaa	22860
gagtgggttaa	agaggcagaa	gaatcagaag	agaaccagat	tcatgaaata	aaagagagga	22920
atcagtttca	ggaaggaaag	tgtgggtcagt	agtgtcaaat	accasagact	gaatagycta	22980
aggattttaa	agaggtcaac	agcwccacca	attaagcggg	ttttctgagc	ttaagatatt	23040
tttctttatt	tttctatgtt	aaaaatattt	tataaagaaa	aagaaaaaaa	gagatcacat	23100
ttgccccccc	aaccctgtccc	tggcctctct	ctctctaagg	aagtcgttaa	tgaatttggg	23160
cagaatagat	tcagagctgt	gagagtga	atttgactgc	agtgggtgag	gtgttaataa	23220
aagggagggg	gtagagatga	aatcttttcca	gcagtttggc	tcttaagggg	atagcttgaa	23280
ggaaagaggg	ttggaagggt	ggttttttaa	aagaattatc	actcactaat	caactagaaa	23340
tccagtgga	tatgcagtac	ttgtctgtaa	tccagcaggc	taactttttt	tttttttttt	23400
ttttgagacg	gagtctcgct	ctgtcaccca	ggctggagtg	cagtggcatg	atcttggctt	23460
accgcaacct	ctgcctccca	gttcaagcaa	ttctcttgcc	tcagcctccc	aagtagctgg	23520

aactacaggg	atgcaccacc	atgcatggct	aaattttttt	tgaattttta	gtagagatga	23580
gtttcaccat	gttggtcagg	ctgggtctcaa	attcctgacc	tcaagtgatc	acccgcctca	23640
acctcccaaa	gtgctgggat	tacaggccag	agccacagtg	cccagccaag	gctaacctct	23700
tgatcccaat	gacaaacaga	acaaacatct	tactcaagtc	cagaagcaat	aataattttg	23760
aatcttgctt	gcatgtcaac	aggagccaca	ttaatacaga	agaggatcac	attgggtccaa	23820
ttaaattgaa	ttgattgaga	gcctctgcaa	tacacgggtct	actgcacaaa	taatgatggg	23880
tcctgggtaca	tttttatttg	accattgatt	gctcgatttg	tttctgtgtc	taactgtgta	23940
ttggaattaa	gctgactcaa	tttgaactgc	aggctccttt	atccctctta	ttttttattt	24000
atttatttat	tttattttta	ggcattttctc	actctccaga	aaatctctaa	gattttcagct	24060
attaggcatt	tgtctttttt	tttttttttt	tttttttttt	tgagactgag	tcttctggg	24120
ttgcccaggc	tggaatgcag	tgtcacaatc	tcgggtcatc	acaacctcca	cctccctgat	24180
tcaagtgatt	ctcctgcctc	agactcccga	gtagctgtga	ctataggtgc	aaaccaccna	24240
cgcccagcta	atttttgtat	tttttagtaga	gacagggtttt	cactatgttg	gccaagctgg	24300
tctcaaactc	ctaacctcaa	gtgatctgccc	cgccctggccc	tcccaaagtg	ctgggattat	24360
aggcatgagc	caccgtgccc	caccaggtct	tcttaatcat	aacaaaattca	tcttaaaaaca	24420
tcatttttaa	atatattatt	ttttattctt	cattgacttc	ctgcattact	ctattttttt	24480
agagtttcta	gcaaccagta	tcattgggtat	tttaaacat	gtgtacatgt	acattttatgc	24540
agatgagtta	acatatatca	aagcaacctc	caaacatgct	catttaggta	atctccaatt	24600
taaaagcctc	aatagaatga	taagattgag	cttttctgta	gttccatgac	ctccagcaga	24660
gtctgcaagg	ccacagctgc	ctgaagggtg	attctgtaat	tagaagatgc	cagggtcatc	24720
tcagaataga	acctcaagcc	acccaggcta	catttacaga	atcagcctct	ccagaaaaac	24780
agcaacaaag	gagggccttc	ctatgtattt	ggaaggagtc	acctagagga	gggacttggg	24840
gttttgggtg	tggtgtgggg	ggcagggatg	ggatggggag	ggggaagctt	attgaaatat	24900
actaaaagac	aaaccaacct	aagggctgga	gggaagaaaa	ttcacacttg	taagcttctt	24960
ttttaagggg	catctcttag	gctctagctt	ttgagattca	gtatatatat	atttttgagt	25020
cttgctctgc	tgagtgagc	tggtgtgatc	tggtgtcact	gcaagttctg	cctctcaggt	25080
tcacaccatt	cttctgcctc	agcctcccga	gcagctggga	ctacaggcgc	ctgccaccat	25140
gcccagctaa	ttttttgtat	tttttagtaga	gacgggggtt	caccctgtta	gccaggatgg	25200
tctcgatctc	ctgatctcat	gatccgccc	cctcggcctc	ccaaaatgct	gggattacag	25260
gcgtgagcca	ccgcgcccgg	cccagtattt	ttgttttatg	aagatattac	atttgtaaag	25320
tatgagcttg	gtgtcagcaa	acttatatcc	ctgtgtacaa	actggccgaa	tcacttagcc	25380
actttggggc	aaatcactta	gctcttctaa	cagtaagaaa	tcaacaagaa	aaataaacat	25440
ttcaaacatt	acaatgtgtt	catgtattca	ctgtggggga	tgaccagatt	ctcgaaacca	25500
cagggtgttc	ttagtgaac	aagtttgggt	tggggccata	gacttgtgta	tttagaatca	25560
atggctgttc	tctctctggg	actttgattt	ttttcttggg	ctcatccctt	ttttgtagta	25620
tcttatcttt	gtcttatttg	tataggactt	aactgttccc	attcccttat	tagagcaatc	25680
taagtgatta	ccttcatacc	ttttggaatt	atatgttcca	aaattccaaa	aagaatgatt	25740
ttgggctggg	cacagtggct	cacacctata	attccagcac	tttgagaggc	tgaggtggat	25800
cgctgaggt	caggagtttg	asrccawcct	ggccaacgat	agtgaacccc	cgtctctact	25860
aaaaaatata	aaaaattagc	cgggcatggt	ggcaggtgcc	tgtaatctca	gctactcggg	25920
aggtggaggt	tgcaatgagc	ccagatcgca	ccattgcact	ccagcctggg	caacaaaagg	25980
tgaaactcca	tctcaattaa	aaaaaaaaata	atgatttttg	tggtcgactt	caaataggta	26040
ggagaagaag	gagagaggag	atggagggtc	asggagatct	aattactctc	taaaatcatg	26100
ctaggaaaga	taacaccttt	taataacact	ctctgctttt	ataacatcat	tctgccagg	26160
agctcaaagg	tttcaacama	gttcactttc	agaaaacccc	tttgaggaag	acagaatata	26220
catcttctct	ccmtttttaa	gatgaagaaa	caggccgggc	acaatggcta	atgcctgtaa	26280
tcccagcact	ttkggaggct	gaggccasar	gatcgcttga	gctccaragt	ttgagaccag	26340
cctggataac	atggcaaac	cctgtctcta	caaaaaaat	acgaaaatta	gatgggtgtg	26400
gtggcatgca	cctgtgggtc	cagctacttg	ggaggctaag	gtgggaggat	cgcttgagcc	26460
cagggagtc	agtctacact	gagccatgat	tggtactactg	cactccagcc	tggttagaca	26520
gagcaagacc	ctgtctcaaa	caaatgaat	gaaagagaaa	gaaagaaaga	gtgagaggag	26580
aggagatgag	gggaggggag	ggtagcagg	agggggggag	gaagggaagg	aggaagggaag	26640
gaaaaaaaga	tgaaaaaaga	aatacgcaac	atgaaacaga	ggcagaaaga	ctttacgtaa	26700
attgctcatc	atgtggttgt	caagtttgac	cccaaacccc	aattttattga	ccaaggttat	26760

tctttgactg	aggcaagggg	gtccgctctc	ctgggccttg	ggcttttagaa	agctcatctc	26820
tggcctttct	gagatccatc	cctttctttt	tatttttctt	gacacggagt	cttgctctgt	26880
cactcaggct	ggagtgcagt	ggcatgatct	cgactcactg	taacctctgc	ctcccgggtt	26940
caagcgattc	tcttgectca	gcctcctgag	ataacaggcg	ctcgccacca	catctggcta	27000
atttttgtat	ttttagtaaa	gactgggttt	catcatgttg	gccaggtttg	tttcgaactc	27060
ctgacctgag	gtgagctgcc	caccttgccc	tcccaaagtg	ctgggattac	aggcatgagc	27120
cactgcgccc	agctcagatc	catccctttc	taaggggcaa	cagtcctatg	tgcaaagggg	27180
ccatgccacc	cagagttatg	agtacctggg	actccagaat	tccttgccctg	gtggcctcca	27240
catgcacttc	cagggcctgc	ttgggcctct	tctatgggtc	tgtcctgagt	gttgatagaa	27300
ccactgatgt	gagtaacctg	gcttgagccg	tggcctggag	atcctgttga	ctgtagcatt	27360
gagggggctt	gtgcagctga	atgtctgyat	gcagggtggtg	ggagtctctg	aatatgatgg	27420
agctggagggt	gggaagagaa	gtaggcttgg	ggcagctctc	tcatgccacc	tcattctggc	27480
caaaactcag	gtcaaactgt	gaagagtcta	aatgtgaatc	tgcccttcaa	gggtggctaca	27540
aaggtatctt	tgtcaaggta	ggagaccttg	tggcctccac	gtgcacttcc	agggcctgct	27600
tgggcctctt	ctacgggtct	gtcctgagtc	tctatgnaa	tctgtccttc	agggcagatt	27660
catattttaga	ctcttcacag	tttgacctga	gttttggcca	gaataagggtg	acatttagtt	27720
tgttggccttg	atggatgact	taaatatttta	gacatatggg	gtgtaggcct	gcattctctac	27780
tcttgccctt	ttttttgccc	ctccagtgtt	ttgggtagtt	ttgctccctt	acagccaaa	27840
gcaaacagak	aagttggagg	tctggagtgg	ctacataatt	ttacacgact	gcaattctct	27900
ggctgcactt	cacaaatgta	tacaaactaa	atacaagtcc	tgtgttttta	tcacagggag	27960
gctgatcaat	ataatgaaat	taaaaggggg	ctgggtccata	ttgttctgtg	tttttgtttg	28020
tttggttctt	ttnnntnnnt	nnntgttttt	gtggcctcct	tcctctcaat	ttatgaagag	28080
aagcagtaag	atgttccctc	cgggtcctct	gagggacctg	gggagctcag	gctgggaatc	28140
tccaaggcag	taggtcgccct	atcaaaaatc	aaagtccagg	tttgtggggg	gaaaaacaaa	28200
gcagcccat	acccagagga	ctgtccgcct	tccctcacc	ccagcctagg	cctttgaaag	28260
gaaacaaaag	acaagacaaa	atgattggcg	tcttgaggga	gattcagcct	agagctctct	28320
ctcccccaat	ccctccctcc	ggctgaggaa	actaacaag	gaaaaaaaaa	ttcgaggaaag	28380
caggatttag	aggaagcaaa	ttccactggg	gcccttggct	gccgggaacg	tggactagag	28440
agtctgcggc	gcagccccga	gcccagcgct	tcccgcgct	cttaggccgg	cgggcccggg	28500
cgggggaagg	ggacgcagac	cgcgggacct	aagacacctg	ctgtaccctc	cannncnnc	28560
ccacccacc	cacctccccc	caactcccta	gatgtgtcgt	gggcggtgta	acgtcgcccg	28620
tttaaggggc	gggccccggc	tccactgtct	ttctgtctgag	tgactgaact	acataaacac	28680
aggccgggaa	ggggcgggg	aggagggaga	gcacaggctt	tgaccgatag	taacctctgc	28740
gctcgggtgca	gccgaatcta	taaaaggaac	tagtcccggc	aaaaaccccc	taattgcgag	28800
cgagagttag	tggggcccgg	acccgcagag	ccgagccgac	ccttctctcc	cgggctgcgg	28860
cagggcaggg	cggggagctc	cgcgaccaa	cagagccggt	tctcaggggc	ctttgtctct	28920
tgttttttcc	ccggttctgt	tttctccctt	tctccggaag	gcttgtcaag	gggtaggaga	28980
aagagacgca	macacaaaag	tggaaaacag	gtaagaggct	ctccagtga	ttacttgggc	29040
gttattgttt	tgtttcgagg	ccaaggaggc	ttcggggaagt	gctcgggttc	ggggactttg	29100
atccggagcc	ccacatcccc	accacttgca	actcagatgg	gaccggaggc	ggtgttaaat	29160
ggggagacga	tgctctagta	cgagctctgg	tgaccccgag	actctgcgct	gctgcgcttg	29220
ngggcttgcc	cgacgggtgga	gaccggggag	catctctggg	cgtggagacc	cgggcgcagt	29280
accccgggct	cagaggggtc	gggggttccc	ggngcgtgct	gagggcgctg	ctgcgggtg	29340
gggagagctg	caggtccggc	accgagncgc	tgctttgttc	ggagggccct	gagctggcnt	29400
agnaaaccct	tctgggttga	ggtcggccag	tacctacgga	gacaaatgcc	agcactgagt	29460
cttcaactcg	ttcttaagaa	gctgggtctgt	tctgacctgg	gaattggcta	tatgctcccc	29520
gggactggag	cggcacagtc	ccggactgtg	aatccgggaa	ctcgagttag	aggtgtccca	29580
aacgggtccgt	ggtgctattg	ctcactagag	gccttgggtc	tttgntttga	cctgaggggt	29640
agggaggtcc	tgccctacagt	ctccgtgcgc	tcagctgagc	tggtgtccct	ggcgagagc	29700
gcggacgagt	tttggttccct	tttctttttc	ttttttttct	ttcctttaag	tctcggtctg	29760
tcgcccaggc	tggagtgcaa	tggaaacgnat	ctccgctcac	tgcaacctcc	gcctccccgg	29820
ttcaagcgat	tctcctgcct	cagcctcctg	agtagctggg	attacaggcg	cgtcaccaca	29880
tccagctaata	ttttgtattt	ttagtagaga	cgggggttca	acttgttggc	caggctggct	29940
tcgaaccctc	gacctcaggt	gatccaccgn	gcctcggcct	ccccagtg	tgggattata	30000

```

ggcgtgagcc accgcgcgcg gccgagtttt gtttctttta aaaacaagac ttaggagagc 30060
ctgcggagac ccggagggtgg ggtgcccatt cctccctctc ccacgttccc tgcagcccca 30120
tcttccagac cgttgcgtct ggtctctcgg ggcagcttct gcctggggcg agatggggaa 30180
gctgggcccga ggtggtgccg tggaaatgacc gggagtaacc ccggcggggcg gcgcagaact 30240
cggagctccg ccgcggggct gggctgggct ctgccgtgag ggtgggggtg ctgggcgcgc 30300
gggctgcggg ggnccccgga gactggcccc ctggccggag gacctaggaa 30360
tcggccgggt ctactagggt tctttgctcg cggttccgac tgtgaatccg gtgaagaccg 30420
gtgggttgcag acggggagga actatgaggt tgaggcgaaa gcccgttttg tttttttttt 30480
tttgtttttt tggttttttt ttttgtttag gtggttgcca actcccaggc cattggtaaa 30540
gcagggaagg tcttggggcg gcggacggtg ccagggttat gtgtagggtg ctctttagg 30600
atatctttta tcaaaaagaa gcaaaagaaat aagattaaaa ataaacaaag aaaaaagttg 30660
tctggcactg gcagtaattg gcctgccttt gcagcactga taccattagc ttttaaaatc 30720
cgacttttca ttgacacttc aagaagagaa tgggtagtat atacacattc atctcatagt 30780
ggacaaaatt catattttaa aaaaccttct gggtagtgaa atcagcaagt cacttgccct 30840
ccatggccga atccctgctt cccacgaaga gaacctcaca aaaatttccc ccaagttaaa 30900
gagtgggaatt tcttgattt tttntttctt ttttttttaa cggccgtagt ttagaanccc 30960
agacttaaat tatgatcttc ttttcaaaca aaacttaaa tctttaagtt ttcactcccc 31020
cttttatttc aacctattct tctcatacct accacaaaa taatggaggc tttctgttga 31080
gaaactttcc gtttctgttg agagtatcat tctcttgaga aactttctcc taaatcagag 31140
aaagtattga agcatggaaa gtattcctga gtagaacctc tacagatatt acaatatttt 31200
tcaaatacaa agtttccatt gtcagcctgt tcccaagtg cttccacaaa ccattaaata 31260
attccacaaa ccattaaaat aattaatgct agggaaattt aggaaaacat tggtttacia 31320
tcagaaggac cggggaagtg ggtcttcagc cttcacgatg actacaagcc atttaaggga 31380
ctagaattgc tactgttgtc agagcaattt aggaagtctg atttgagcac ccgcatagtg 31440
ttccagaatg acatatctga ctgtaacctg gacacgtgtg atatgttgtc tcccctgcag 31500
atgagcattt gaaatctcaa cctcgtatt tctacgagtg caggcctata atggaccctg 31560
ggcacatttt tttttttttt gagatgcagt ctgcctctgt tcccaggct ggagtgcagt 31620
ggcacgatat ggctcactgc aacctccacc tctgggttc aagagattct cctgcctcag 31680
cctcctgagt agctgggact ataggcgcac gccaccatgc ctggctagt tttgcatttt 31740
cagtagagac agagtttcac catgttggcc aggatggtct cgatttctctg acctcttgat 31800
ccacccgcct cggcctccca aagtgcctggg attacaggcg tgaggcaccg cggccgaccc 31860
ctggacacat tttgacttag aacatatttt cggtttgtgt gagacagtgc attagtgcag 31920
gagtggaaaa gatgatcag gaattgattg ttttcaagga ttggttcctt ctgctcaagg 31980
aagtcccat gtaaacataa aaaaatgaat gaaactgaag aagttcagt acttagcttt 32040
ttattatctt ctgtagtact tacctttttg gagaggagt ggttgggata tttttccatt 32100
taaatttttt ttttaaaggg atcttctctc ccgtaaagcc ggatacttaa gctatatatg 32160
tagtggctac aaattaaggc cttcactggt ttcattttta gctgctagaa taagtgaaca 32220
ttaccttaga tagactcttc taattatgaa gatctctaga tgtctagaaa atatcaaat 32280
gcatgtggtt tttgcatttc taaaataact ttaaaaccaa atactttttc tttttttttt 32340
ttttctgaga tggagtcttg ctcttttgcc taggctggag cgcagtagaa tgatcttggc 32400
tactgcacac ttcgcctct cagggttcagg tgattctcct gcctcaacct cctgagtagc 32460
tggtattaca ggtgcgtgcc accacacccg gctagttttt gtgttttttag tagggacagg 32520
gtttcaccat gttggccagg ctgggtctcaa gctcctgacc tcaagtgatc tgccagcctc 32580
agcctcccaa agtgctggga ttacaggcat gagccaccac acctggcctc aaatacattt 32640
ttttaagtat ccagatatta aataaataat accattatag tagttgttat ggtcatttac 32700
tctagcatca aatgttaaaa gatcattctg aacacttggt ttgtttatgc tgagagaagg 32760
cctactccaa aaaatgcaac catcttcgta tctgcactgt gatacaacca tgaatggcca 32820
aagttattgc agtggtgaat agacacttat atagcactgt gtggcaagta ctggttgaaa 32880
tggttttcac gtgtttatct attgtattta ttttgagata gggctctgct ctgttgca 32940
gggtgagtg cagctgcaca gacaaggctc actgcaacct cagcctcctg cgctcacgtg 33000
atctcatata atcagcctct taaggagctg gggccacagg cacgcaccac tgctcctggc 33060
taaattttta caattttttg taaagacaag gtctcactat cttgctcaga ctggtcttga 33120
actcctgggc tcaagtgatc ctccacatc agcctcccaa agtgctggga ttacaggcat 33180
aagccactgt gcaggtcatc aaatgcta tgaattttca caacaaaacc atttattgtc 33240

```

cctagtttac	aagattaagt	aatgagaag	ctaatttttc	tctggctata	taccttgcaa	33300
gaggcagagc	taagacttga	acccagccag	agttctttta	ctccagcact	aacatttcag	33360
ctgctgcaac	cagggagcct	ttcaaggatg	atcaccacat	tctctacatt	catctgctat	33420
aatcctttatc	agaatctaca	gcctgtatca	tattttcctt	gttgctgtga	gtgggtcagc	33480
caaattctct	ttaacttgaa	accttggttg	cgtagggttg	gcaacatcct	ggaaagaata	33540
gaataaaaatt	tactcaactc	aattttttac	ttggttcata	atgaaaacta	tactattgct	33600
tcagtcagat	gtttgccaat	agctgtgtga	tctcaaaatg	ttttcctatg	tgatctatag	33660
naaaaatggaa	tgatagagta	ttaggctgta	agggcctaag	anaacaaagg	aaaaagagaa	33720
gtgaactgtt	agtttagttg	taaaacctaa	ctttggtgaa	ttgtaaaaat	ttgttataat	33780
acaatatgat	tcttgcttgt	cctgtccttg	atgaagtgtg	ggaccttttg	aaataagcta	33840
tttctctgtt	actgctgtta	ctgttttaga	atcaaattta	gttttttctt	aagatatacg	33900
tatttttggg	agataaacac	agtttcaaag	tctgccttgt	tggctgggtg	cactggctca	33960
ttgttctatt	cccagcactt	tgggaggcca	aagcaggagg	atcacttgag	gntcaggng	34020
ttncagaacn	cagncctggc	aaatatgggtg	aaaccccgct	tctactaaca	atacaaaaat	34080
tagctgggag	tggtgggtggg	tgcttgtaat	cccagctact	gggattggga	ggctgaagta	34140
gaagaattgc	ttgaacctgg	gaggcggagg	ttgcaactgag	tcgagatcgt	gccactttac	34200
tccaacctgg	gcgacagagt	gagactccgt	cttgaaaaaa	aatgtctgcc	ttgtaaaagt	34260
gaaataggat	gagaaagtgc	ctttcttatt	aattggtgta	atgaattaga	aataaactct	34320
ttgaagacac	ctcttggtta	aaatagttac	atttactgtt	gattttatgt	atgttgagta	34380
tgtttttaag	ttttccgtgt	aataactcag	ttcattctca	tgagtgaat	aggtgctttt	34440
attgtcttta	tagatgggaa	actgaggtat	agggaggcta	ggtacattat	tatggagttc	34500
gtaagtagtg	gagctgaagt	cgcacccag	acagtttggc	ttccgtgagt	ttaccaatct	34560
catggtaaaag	actttgtcag	actatcaaag	ttttgacaaa	tgaaatatta	gcaaaaggcc	34620
aaaagggtat	ctctattttc	atttgagtat	cttcacctga	aaatagttgc	ctgaataagt	34680
agcctgcata	gaaaggtaca	ttttagaaat	acttgaggcc	agagaatgaa	aagcttacat	34740
aaaaattgatt	tccggtgggg	ccttcagtta	ctctccattc	tacgaagacc	acaaatagca	34800
ttcaggcaaa	gagcatttat	tccaacaatg	gaggagcact	ggattttggt	cctaaaaaca	34860
aataaaagttt	gaaatcctgt	ctttcccatg	ttgaaaaaaa	agttggtaca	aaacccctta	34920
gcttttgcaa	acctccttta	agacccgatt	taaatgcytc	cctcctcatg	aagctcttct	34980
ggatccactc	yttcccatca	ctaagttgaa	agtaagatcc	ccttctcttt	acttccatta	35040
gacttggtat	acagcactct	ttgtatcatg	tatttaattc	tgttttttta	ttacagttaa	35100
catttatttg	tcttctctt	gagtgtatgc	tctctagag	gaaggctctt	gattcattct	35160
cccctggcct	taattcatcc	cacttaatat	ggaaaaaatt	taataaatgc	tgacttgaat	35220
aagtccaaca	aggagaatgg	gaagctcatg	tttgcttctt	gtcttctaaa	agactactta	35280
agataacagg	gtaatcacag	aaaagcatta	gaaatagagt	tatatgagaa	acaactgtag	35340
ttaaggctag	gtttatgta	gactgagaaa	ttttagtga	tacttaagtt	atttaggcca	35400
ggttactttt	tgtagaacia	acatttcagt	ttcgctcagt	ttcattttccg	ttctgnagg	35460
cagctgtgat	ttaagaaaat	gctctagtct	gtggcattcc	atattcaagt	actttgagtt	35520
gtatattaat	ttatttttgt	taataagagt	gacatgactc	actaagtaat	ttagagattt	35580
aaacactttt	ttaaaaaaca	gtaacttcat	atgcattgga	tctattcttc	tataaagtct	35640
tttcttgggg	ggtgtttgtt	taaaattccc	cgggtgtttc	tctgccaat	ccaacttcca	35700
agaagcattt	ggaagtcaaa	acattttatc	tggttagtct	taaagtccag	atattttgtg	35760
atagctggta	tttagtttat	gatatttccc	aggaagaact	ttttagtagt	tgaaccattt	35820
atgaaagact	tccttgaagc	taccttagag	agttgattta	gttcttcccta	aataagtaaa	35880
tagaatatta	gtattaggac	atcttggagt	atagatgcaa	atattggtga	aaaagaacat	35940
ggatatcaga	gtcaaattaa	tgtagattgg	aattctggtt	attactaatg	gatattctgac	36000
attaggcaag	ttgctgatca	ctctttgcct	cagtttcatc	atctgtaaaa	taggtatttg	36060
tgtttggtga	taatgtgaac	cgtataatat	aatgcttggc	ctatagtga	atttattcat	36120
acgagtgttt	tcagtgattt	taaaagcttg	ctttaggccg	ggcgcgatgg	cttctgoccta	36180
taattccagc	actttgggag	gccaagggtg	gcggatcatg	aggtcaggag	ttcgagacca	36240
gcctgaccag	catggtgaaa	ccccgtctct	actaaaaata	caaaaattag	ctgggcgtgg	36300
tggtgcaagc	ctgtatctcc	agctactcag	gaggcttagg	cagaagaatc	gcttgaacc	36360
aggaggcaga	gattgcagtg	agccgagatg	gtgccactgc	acagagcgag	actccatctc	36420
aaaaaaaaca	aacaaaaaca	aacaaaaaatc	ttgctttata	gtttacttcc	acatcaaat	36480

gtctttatcc	catgttactt	gcattgatat	cccagacatg	aaaagaaaaa	aagatgataa	36540
caatgacagt	tattaaatta	ggttccactc	ttattctaga	tcaccaattc	atattactat	36600
tcagacttgg	aacattaaat	tttagttaa	ctttttttca	aatatgcata	taattgtcag	36660
tggttactat	attttgggga	agagattgtt	gacttctttg	aagaaagata	cggattttct	36720
cttcagaara	aatacacatg	ggctcatata	atccaaattt	tatgtgtaat	tacagggtgt	36780
tcataaatgc	ccacaaatcc	attaagccat	gtgaccttgg	acaagtcatt	ttacttttct	36840
gttttttagg	ttgttgggtc	gtaaaatgat	actacttgac	ttttaaagag	cccttcaagc	36900
tcttatgtcc	tctaacccea	ggctctgtatt	cagaagaagg	ggtgggtcctt	taattagagc	36960
catctagaga	tctgaggaac	atgctgggca	ttagtgtaac	ataccatgtg	gatttttgaga	37020
ggtaaagaaa	aaataaccag	ggaatgcctc	agagcattcc	tgatcagatc	gatgacagaa	37080
gaaaggaatg	agagggagga	gaggaagctg	ttgaaatttc	ctatttacct	gctttgagtg	37140
aatgaagatt	tgaatcatag	aaccagaagg	ggttctcatc	tgaaatgcaa	aggaaggagg	37200
agttgggtta	attcaataag	tttcagttga	gtaaacatga	tttagtgaga	tactgttctt	37260
gcttctgact	caccatttgg	aaaatctctc	taaaataaaa	ttggactctc	catctcggac	37320
atcatttttg	gtgtagggtt	tgcttttttt	tttgagatgg	agtctcgtta	tggtgccag	37380
gctggagtg	agtggcgcaa	tctcggctca	ctgcaacttc	cgccctccag	attcaagcag	37440
ttctcctgcc	tcaacctcct	gagtagctgg	gactacaggg	gtatgccacn	catgtccggc	37500
taatttttgt	atttttttta	tagagacggg	gttttactat	ggtggctagg	ctggtcttta	37560
actcctgacc	ttgtgatctg	cccaccttgg	cttcccagag	tgctgggatt	acagatgtga	37620
gccacagtgc	ccggcctaag	ttttacttct	tataatggac	tccgtttaag	ccaatagggtg	37680
atgaaaggaa	accataacca	actcttcagg	ctcattcatc	cttcaagaat	agcatgctag	37740
taccatcct	aggaggagaa	ttggactata	cctcatgagg	atagtttgaa	gtatctcaga	37800
agaccctcac	tgggggtagg	tgggtaagac	acaaagcttt	ctaaagcact	gtaccaaatt	37860
tgttgtttga	gagatcataa	caaattagaa	gtggaaagaa	gaaggagtaa	aaggaagaag	37920
aggtttctgg	ccaggagcag	ggagggggaa	ggagctgcta	ggaagatgtt	tggttgtcat	37980
atccctgttc	acccttgctt	tgcaaaattc	ttgtaggatg	ccagggtggg	agtaattgtt	38040
tttcacaaga	gtcaaaccac	gcttggtttt	ttgaagaagc	aagtcttttg	aggggtgggtg	38100
cttgaaatct	ggttgatctg	gtatttaggt	gatacacctt	gacataaagg	ncaacactga	38160
tgcaagcagc	agctttcctt	ggaaaggcag	ggagaaagtg	aaggcccaga	ctgatgagct	38220
tacactgacc	tgacagacct	tctccattcc	caggcatggt	tggtggcaga	gtttacctta	38280
gttgggggtta	ggctgttgtc	tggtactgtg	agagagaagg	aagaagaaga	tatgatatta	38340
acaacaacaa	tacatatatta	tatttgaaaa	ttaaatgcac	taatacacct	atagtgtat	38400
taaaacaaat	tatttgttca	gcaaagtgtt	gttaaaccac	aatgtactgt	ggaaagtact	38460
aggtgctgga	cagaggtcaa	aagacttttt	aagaatctgc	caccattaat	gatctctttc	38520
tgcttggcat	tcaaggctct	ttgaaataag	actgtgaccc	actttgatag	ttttgtcctg	38580
gattataaga	cacatgctcg	aaggaactat	agctgggttt	ctcaccagac	tgattaacat	38640
atagtatgg	ttggtacctg	ttaaatgagt	ctctctctac	aggttttcat	cttctacttt	38700
aagaacccct	tccctggcatt	gtttggctcc	tcattgttct	ggaatctcat	gtccatctca	38760
tgtatttggc	ttgggtcaca	cttgatcttc	tgctcatatt	cctcacctac	tgaaatttta	38820
cccatacaacc	agaccgtggg	tgatggaaca	cagcatgggc	tagttcttct	tatatatgat	38880
ctcattttaa	tttactgga	actctgagat	aggtagcatt	tcagcccact	caagttgact	38940
caaatttttg	taatcatcaa	tatattttaa	aataacttta	tatttgacct	gtaattggaa	39000
aaccaatatg	agttatcata	aatgaaaggt	aatttttaaa	ataattagga	tgaagacaaa	39060
ttatttttct	cacagtctat	gtataagata	aactattggg	tcccaaaggc	cccagctgac	39120
aatgagactt	ctcttacttt	gttgaaaagg	gaattagcaa	gcattaaaga	ggtgtcaaaa	39180
agaagactaa	acaaaagctt	actccttttt	ttttttgaga	cgagtcttgc	tctgttgccc	39240
aggctggagt	gcagtggcac	cacctcggct	cactgcaacc	tcttcctcct	gggttcaagc	39300
gattctcctg	cctcagcctc	cctagtagct	gggattacag	gtgcatgcca	ccacaccggg	39360
ctaatttttg	tatttttagc	agagatgggg	ttcgctcatgt	tggccagggt	ggtctccaac	39420
tcctgacctc	aggtgatcca	cccacctcgg	cctcccaaag	tgctagaatc	acagggtgtga	39480
gccgccgcac	ccggccgctt	actccttaat	gtactaagaa	tgttatatat	aggctgaaga	39540
agtgtctgaaa	agaaccatat	tttctcatga	tgtggttcaa	tgtttaatac	tgtgcttgct	39600
catctcctaa	aatcctctga	atatcactta	aattcatcct	gtgtaactct	cccacatttg	39660
gggaaatact	gagcttgcc	attattatat	tagccccata	tttcagatga	tgcacctgag	39720

ccgaggagaa	gttaaataac	ttgttcatgg	ttccatattt	ggctaattggc	agagccaggg	39780
attcaaactc	ttgtctctct	gactcccagg	tttgtgcttt	tcccacttgg	ctgaatttct	39840
catgctacct	cctccataac	acctttcccta	gaacttttaa	ggaatgcttc	ccctgttctc	39900
tcatagcatt	ttaatgtaag	ttgccaagt	gtcccagttt	gcacccctac	cagcaatgtg	39960
ggagaaaata	gcaacatatt	tttgaatgtg	gggtctagtg	ttacggtttc	ttctgtctct	40020
tgggatgtat	attccatggc	tactgaatac	ccaagtccca	aacagttttc	ttagactcag	40080
aaggatcatcc	acttcagctt	cttcatcaaa	aagacatatt	ttctggctgg	gcacgggtggc	40140
tcacacctgt	aatcacagca	ctttgggagg	tggaggcagg	agaattgctt	gaacccagga	40200
ggctgaagtt	gcagtgaacc	cagatcgtgc	cactgccctc	cagcctgggt	gacagagcga	40260
aactctgtgt	caagaaacaa	aaaaaaggac	ttgttttctg	ttccattacc	cacagtggta	40320
gaatggcgtg	ctaaatttat	tctccagctg	ccattaaactg	caaattaaaa	tcttagtctc	40380
ttgcctcttt	aatccaggct	tcttcatact	ataccagaat	ttaggataac	tattacagtg	40440
cccttttatag	gagagaaaga	agaaattgtg	tctgtagatg	tctgttccct	tcagcttaaa	40500
atggacactg	aaatgttaaa	tattggactg	gcctcattta	tttctcctgt	ctgttgggtcc	40560
aatctgaatc	ttaaggcgct	tttcaactgg	aattttttgt	ttctctcaac	taaaaattgt	40620
tctttgtaag	tttgaatcag	aacaaaatcc	tgaatgttga	gggtttcccta	aaggctgttt	40680
ctttatgcaa	aagcctgaaa	cccgatgttg	atgttggctg	cttaaaatta	actgtgaatc	40740
aaggcagggg	ttttattttt	attttttttt	tactttaatg	attgtgttaa	ttatagttaa	40800
aaccttgagt	tcacgagaaa	gaaagccttt	gggtcaagtat	tgtttattaa	gttgtcagtc	40860
ttgttgtagg	atttgcaaat	ttagtggaat	tagtgccatt	tttcagttta	caattccagt	40920
cacatttcac	atgatcagag	catggcttcc	ttctctgtgg	agcaaataga	gggtgtgtctg	40980
acacttgggt	ccagtggctt	ccattaagca	gagtggatat	gtccctggag	tctgcagaga	41040
agggcatggc	actctgaccc	cagatggcac	tccgttttgg	gacattgtcc	aattctagtt	41100
catagcatat	gtgaccaaca	ccagctctca	cctgatgtaa	acacttagcg	cgttgttgct	41160
tgggggattg	gatttgtgtga	atttttcaaa	actacagttg	acagaaggag	gctacaaaaa	41220
atgaaaccca	ataattccat	ttttgggaat	tattcccact	tttgttccat	ttttcccact	41280
ttgttctttg	gcacacagaa	tgtttgattt	gtgaaaatct	taataacagt	agttttttct	41340
ataaggaata	ctcagaatct	tgataatatt	ggaataatac	agatoccttt	gtaggatcct	41400
ctcagacctc	atataataga	gttcatgtag	tcaatattta	aagaaaaaca	cccttaagtt	41460
tttgtttttc	agaatcacia	gtaagtggat	ttaaacttgt	gatcttattc	ccctttcttc	41520
tcttaattta	gtgaggcagc	cagcgagagg	gtttgttttg	gttatcttaa	agaaggagtt	41580
tgcttgtaag	ttttggaggg	caagacttag	actctgtgtc	tctgtgcttg	ccctggaaact	41640
ttgattaaat	tgctactaac	cgagttagct	ggccctcgcc	gggtctgcaga	aatagaagtg	41700
tcttgccacac	atgacatatg	actgtctcaa	gagctggctg	gtgaaaggac	gttctggaga	41760
aggctgccga	tactgtatga	actagaanct	ggacaagagc	ctggagattg	gataactcag	41820
tttggcgcaa	gtaaagggaa	taaaagtgtt	aagggtggcaa	aattgtatcc	aggtgtttat	41880
aggctccctg	agttcctgac	ttgagcctat	ctatgggttt	agagttcaag	gctctttacc	41940
agtgtcgaca	atcttatact	ctagggtgaa	cctccgggga	aggtgccctt	gcttgatggc	42000
atgtttacca	gggtttctag	agcctcaatc	acagattctc	tctagctcac	atgaagttaa	42060
tgaaaatgaa	tgtgcttccc	tacaaattag	agaggctttg	aggaaaaatc	agattaaatg	42120
cactcctgct	tgaacttatg	tttcttagaa	cacagctgga	aattttgtca	cacaaaacct	42180
tactttcagt	gacatttctt	gactggtttg	ttactgtagt	gaatctgctt	taactatctt	42240
ttcttatcgc	tgaggtttta	cttccattct	acatgtgatt	gtggagcgct	gcgtcattgt	42300
gggttcagtg	tagtggagag	taggaagatg	gtgagacaca	gtagcttggt	gcacattgct	42360
taatttatca	gggatcactg	atgagttagt	acactagaga	agattgtagg	tagagctgaa	42420
aagatggagg	aattataagg	ctcagatttc	tctctttttt	ttttttttta	agatggagtt	42480
tcactcttgt	tgtccaggct	ggaattcaat	ggcatgatct	cggtcactg	caacctctgc	42540
ctcccggtt	caagtgaac	ttgatggtct	cacttgatgg	tttctggct	cagcctcctg	42600
agtagctgag	attacaggca	cccactacca	tgcccagcta	cttttttgta	tttttagtgg	42660
agatgggggt	ttatcatgtt	gaccaggctg	gtctcgaact	tctgacctca	ggtgatcacc	42720
tgctcagcc	tcccaaagtg	cagggattac	aggcatgagc	cactgcgtct	nggccaaggc	42780
tcagatttct	aatagagatn	ttctaatgga	catagaggct	ggaggaaatg	ggatnggaca	42840
ngganaaact	gagtncnagg	tgccaaannn	aacttgtagg	gggcccgggtg	cggtggctca	42900
nnccgnccnt	gtaatcccag	cactttggga	ggctgaggcg	ggtggatcac	gaggtcagga	42960

gatcagagacc atcctggcta acacggcgaa acccctgtctc tactaaaaat acaaaaaatt 43020
agccggggcgt gttggcaggc ggctgtcggt agtcccagct actcgggagg ctgaggcagg 43080
agaatggcgt gaagccggga ggccggagctt gcagtgagcc gagatcgcc cactgcactc 43140
cagcctgggc gacagagcca gactccatct aaataaataa atagataaat aaataaaata 43200
aaataaaaaac ttgtagggag gtggcagtggt gctatggagg atagggtgcaa cctctgtgag 43260
aatgtagaga aaatagtata agtgagtggg gaggaccccc aagagggggt tttatagtaa 43320
aacaatggtc agaagtggca acaggatacc gtataatgct ttcacctcta ccaatgcact 43380
gggtactgga gagcgctcca gtttgctctg gaaaggccct ttctgtggac aaagaatata 43440
gaaaagagat tcctttaata aaccaccac tctgtgtccc acccttgatg aatacttcac 43500
tgtgaaattg ccagaattaa tcatggtaat agctactgta cacttacttt gttccaggaa 43560
ctggataaat gttttacata cattatcagt tctatttttt ggagaagata caggggctca 43620
gagtccttag ggttccagag ctggtagta gcagagtcag gattcaaacc cagctttctc 43680
tgactctaaa acctcctttc ttctgtctga aacaattaac tagaccctaa tcaagacaac aaaggagtta 43740
aggattttggg gagttttctg catggtagaa tagaccctaa ggaaaagaaa gaaagacagt 43800
gactaagatt tgggtttgtc tgccccacca aatgctttga gcactttcat aaatataaat 43860
ccttcagggt gggagaaggt tgaacatctg aagacactga ttcttcagag atgtaatcca 43920
aacaagtgta tctttgggtga tatggctact aaacctatta tcccaaaaatt ctcttgga 43980
accgtcctat aacagcagg aacattatcc agccaagttt ttctgcaaat aaagggttgc 44040
tgatagaggc ttgcctgctt gtgtttctng tnagcntnca ggggtgttat gaattcacta 44100
atcccttccc ttccagatccc ttttattctg gtgttatgat tgtgactgna aaaaaattga 44160
ttttttttct atgacataga atgttgaaag gttgatttct ttctagagg aaagattctt 44220
ttttctatg tgctacata cccccgacca gggaaaaggc aaatagtggg attgtttgct 44280
gaagtcttcc tttgaagggt gcttgggtgt ttcttagtgg aaatcagcag gggaagagag 44340
gctatctctn aacattttgt tagangtttc ttcgtnagtt ctatagtga gaaacaagga 44400
cttggggtag aggacagatc tgctttcaga aatcctggct cttgtgaggg ttagaagccc 44460
tgagaccatt tagctggtag caacgggaat gttgaggggt ataaatagga tctttgggtg 44520
tccaagtatc agtgacatga tatagatgga gttaaacctt taggatctcc ttatttattt 44580
gtttgtttat ttttgagaca gggctcttga ctgtagccca ggttgagta tgggtggcatg 44640
atcataactc actgcagcct caaactcctg ggctcaagcg atcctgctgc ctacgctcc 44700
caagggtgta ggattacagg catgagccgc cacaccgggt caggatctcc tgtaaaatta 44760
tattgttgac aacatgaaga attatgcttc tcaaaagcta gttatagatt tgtacaatat 44820
tcatagattt ctgtttcag tttttacaaa ttcctagccc ttattttgaa aattagctat 44880
tagcaataat tttgtctagg aaattggatg tgtattcaag tgaaagaagg aagtacagtt 44940
acctattatc ttattgtaac taacaatcaa gtaagtgtga tgcatttggt actttaaaaa 45000
ctgcacccaa gttacagatt attggaatta ataaaattca ctggatctat atatttttaa 45060
acggacagtg tgatagcaga acctcttata gaatngatag aattcctctg gaatgattgg 45120
ataacttcat ttcatccttg acttttacct tggaggattt cttaccctt ttggcttctc 45180
aaatttgact attaaaatgt tgcttttaa aataggaaca cagtttcagg ggggagtacc 45240
agcccatgac ccttctgcaa ggccccctaa ctcaaggtag ttccctgga actgtggttt 45300
atggaatggt tcaggagtgt gaggaggtat aatttaaggc tgcctagca aggataccct 45360
taaggataga gggcccagta gcatctggag gccagaaaag ttanaactga ggcagtcaga 45420
ttagcttcan ggctcaatta agctgatggg tcagcctggg agaaattgca ggtgactct 45480
caatatcccc tcccaccccc acagcagcca cgatctgtct gtctttaatc atgggtgcag 45540
tgaacctgtt ctttccaggt gtcttggcct tcagtaacct tgttaggctt gtcctgaac 45600
gtggctaccg atccaaagac acatgatcag agaggcaatt agagaacaga ccttttccaa 45660
agcaagcatg ttctgttggg cttagaagtt tcatgtccta atattatagg accctgtgca 45720
tctctctgga gatgaggcac atgagtcata tctgtgattc ttgcttttgt gtcaacatct 45780
catgaatagg caatcagagc tttggacca atgtattttc agttcatatc tgatgtagtt 45840
aatccacct cctgctttgt agtttactgg caagctgttt ttgatataag acatctagaa 45900
cactgtaaat atataacatt tttatttgtc tattatacct caattacgaa aaagacatct 45960
agaagcaacc tcatcaagag agatactgag gccgggcatg gtagctcaca cttgcaatcc 46020
cattactttg ggaggctgag gcaggtagat cacttgagggt caagaatttg aaaccagcct 46080
ggccaacatg ttgaaacct gtctctatta aaaatacaaa aaagttagct gggcttgggtg 46140
gtgggcacct gtaatcccag ctactccgga ggctgaggca ggagaatcac ttgaacctgg 46200


```

gaggcagagg ttgcagtgag ctgagatcac accactgcac tccaacctgg gcaccagagt 46260
gagattacat ctaaaaaata aaataaagta ataaaaaaga gagatattga tagctgttgt 46320
tggaatttcc aacttccatc tcacttctgg taactttttg gaagtttgtt gaacaaagtg 46380
gaatacacgc acatacacac acacacatac tctcttgttt gtttaagggt taatgaaata 46440
gctgtcatat aatcactggt tttgaaagag gagaattagt tgctatctgt acattttggg 46500
tatgtgaact atttgatag aactctgaga aatgcattca gaacaacaaa caaatcata 46560
ggagaaatag ctaagtggga aggggcatat aagagttgtt gaaaaagtta tttcttgaga 46620
aaccagctct aatgctaggc aagtcacttg ctttggggga ggcctcagct tctctgtcta 46680
taagattgca gcaggggtgt agtgggaatg agtcttcaac attccaagag attttatcta 46740
ctaatacgac agtcaaatgg agcatgactt tgtggaagcc tctcctcttc caccagagg 46800
ggccaatttc tctgtcccag tgagatgttg acacttgtat gatccctgct tggagacttc 46860
cctcttctgg aacctgccct ggctcaggca tgagggtgta ctgtcaccct tcgataggag 46920
cccagacata aagctcatgt gttggcagtg ttcttgcggg aagggaaaag accagccagc 46980
ccatttgtta ctgcacaagc aaacagcttc tggtagctgt acagatacat gcactttctt 47040
tcttctactgt gtttccatag acagatttag tgcttagaa gagtagagg cagtcacggg 47100
aaggagttcc tgtttttctt ttggctatgc caaatgggga aaaatcctcc tatcttgtct 47160
tttttagtgc atcctctctc cctttttctt cttctttata attctcatct ctcactctc 47220
ctggaaaatgt gcattgtcaag tcaaaaaggg cacaatgttt tgggtaggaa gaggtgggag 47280
aacacgtgcc aggtgctaac tagggctatc atttccccct tcacagccag cttcctgtga 47340
atgtgtgtgt gtgtgtgtgt gtgtgtgtgt gtgtgtgtgt ttcttttggc 47400
agcatcactg aatctgtctg ctgtctggta ttccagggtt tggtttaggg aaaagtaaaa 47460
gtaattttat aatcccagct gtcatttaag ccaccccntt tgtgggtagc atatggtcca 47520
ctctctcagt tcattgtcct aaagatgctt catcagaaag gaataacttc caccctgta 47580
ctctctgtcc ccttactctg ctttattttt cttcgtcaat cctaccacca ccaccactg 47640
tttgaacaac ccactattat ttgtctgttt cccatccctg gtagaatagg agcccatga 47700
atgaaggaac tttgcttctg ttgttcacca ctgaatctct aaggtatgga acacacctgg 47760
catgtgatag gcactcgata aatatttgtt gtggctcatg ggcaccttgc agagttaagg 47820
ctgcagtgtt ttgtggaatt tataagtggg aatgaatatt tatctactat tctcttcca 47880
aggcgatcac acaataatca ggctttacac tatccagttc ttaggtcttc caagttatga 47940
cttgtgaggt atgttaatta tgataataga aggcagttta tttggttcag atttattgat 48000
gtgtaattta ccacagtaag acttccccct taaaaagta tgatgagttt tgacaaatgg 48060
atacacatgt tatctacca ctgccatgct ccttttccag ctgtcgtccc ctcacccat 48120
gaccactggg caccactgca gtgatttctg tccccttcat ttcacctttt ccagaatgtc 48180
atataaatgg aatcatgcag tatgtagttt tttgtgtctg gcttattttt cttagcatta 48240
ggcttttggg attcatccag gttgtcgcat gtaacagtag cttattcctt tttatggctg 48300
agtaagtgtc ccagttttat ttatatattt atttatgagg aggtgtctca cttgtcacc 48360
caggctggag tgcggtagcg cgatctcagc tcaactgaac ctccgctccc caggttcaag 48420
caattctcct gcctcctgag tagctgggat tacaggcacc caccgccacg cccaactaat 48480
ttttatattt ttagtagaga tgggttttca ccatgttggc caggctgac tcaaaactct 48540
gacctcaggt gatccgcccc cctctggctc ccaaagtgtc aggattacag gcatgagcca 48600
ctgtgcccag ccccagtttt atttattcac cagttgatgg tcttttgcag aactaattgt 48660
ttccagtttt tggctattct gtataaggct tctataaata ttcacaaata ctaggatgg 48720
gatgactggg tcatataata gtactgtata acctagcag aaactgtcaa actattttcc 48780
aaagtggctc ttccatttta caattccaca gtgtattgag tcccagtgct tccatacaca 48840
tgctagcact tttaatattt aatttagtgg gtatgtaatg atatctcatt gtgggtttta 48900
tttgcatttc tctgcagcta atgatgagtg tttctgctta tttgggaagg ttttaattta 48960
gcagtctgtt gtattctgta gatattaata acttcaaaat atcagtggca tttgcagtta 49020
aaatttctct aaaaaattgg ccaaagggtt ccagcagtc cttctgccat gcccactg 49080
tatgaaacaa ggctgaggtg tggagattgt cacattttgg caaggagtga tccacttggg 49140
tgactgatga gaccagaga gcgtacgcct cgggcttgag ggtgaggacg ggcgggaagt 49200
cgactgcagc gccctgctgg ccttgggagg ctgcccagtc cttagctaaa gctggcagtt 49260
atgggaaaca gacttagatt ctattacgtt tttcaggatg tcccaggagt cacc:gggaa 49320
gctcagcagt cctttgtgac tttcaagcat atggtagaag ctgctgaaca cagagctccc 49380
tctttgggga taatttgcct aaatcattta atcaggcttg agaaatgagt taccacaggt 49440

```

ccaggagtgc	tgccaccctt	gaattctgac	accctatttc	tcctatccgt	ctcttaatta	49500
attaagcaga	catccccaag	tgcttacgac	aagccaggac	cctttttgcat	actaaggaaa	49560
acagggatga	aggaaacaga	aatgggtctct	gctctgactc	agaaggtaga	aatcctcttt	49620
cccagccaag	tcttcctagg	gagcacgtag	gaagggtctct	gaacccacgt	gtcagttgca	49680
ggggaggata	tcaggaaaagg	acattgaaga	agtggagacc	taagtttgag	acctaggcat	49740
tagccaggct	agcagtgcct	gaaaaagtgt	cttaggacaa	gagaactcac	cagtgaagtc	49800
ccagtggtag	gagagcgtgc	agcatattct	gagcctgtat	acacatctcc	agggcattgc	49860
ttagcaggtg	gggagtggca	agagagttagg	ctggagtcac	agaaggagg	ccaggtagac	49920
cttgggtgagc	actggactct	atgttcagggt	gctgaggagc	tggcaaaagg	ttttaagtctg	49980
gggagaggca	tggttcagata	tttgggtctag	ctgagtaact	ttgggtgctc	tgtgacaaat	50040
ggttgggaga	ccagttaggt	ggcagttgctg	gtcatctagg	agcaggatca	gagtggccta	50100
ttgactggga	tgactgtgaa	gtgggatccct	ttccagccag	taactggaaa	tgtgtatgag	50160
ggcagaagtg	agtgtactgc	atttgaatac	ttgagaaatc	tagtacatag	tactgtctct	50220
tttatatctt	tttttttttt	tttttttgatt	ttgggtttgtt	tggttcactaa	cttggaatac	50280
tgatgtggaa	atgtcccttt	ggcttcagtt	acctgagcag	aaggggccgg	gcattgccaa	50340
actctcctct	taggacagaa	ttgctcccag	tattgatcat	tgtgttctga	gttgggggag	50400
caaattgtgc	aggaggccag	gtcagtgcca	aggtgggtgg	gaggaattgg	agcagggaagc	50460
ttgccaagt	gtgcccagca	aagccacggt	agaactttct	actgtggctc	tatgtactct	50520
cttagcaacc	ttctccatgt	gcttcctgga	gagtccttgg	agtcagaacc	ttttcttga	50580
aaccagaca	ctttacttcc	aagaaaatgc	tgtccaagaa	aactcatcct	tcccttcttc	50640
tcatgaacgt	tgtgtagagg	tgtgtcttct	cttcctttga	gcttttccac	tcagggttta	50700
ggggagggtga	tattctatat	ttgggtttgg	ctctgggtac	tgcaacacta	ggctattaag	50760
atttcatcct	tactgctttg	cccctcctat	ctttccagaa	acccacaatg	gatttgctag	50820
aaataatgga	acgtcctgtt	tggacaggat	ataaccattt	ctcagctaga	ggatattgtt	50880
ggaatgaaga	aagataaatg	gggagaagg	aactcacatt	gctttggcac	ttaaattaag	50940
ccatgtactg	tgttgggaaa	ttattttatat	tatctcgttg	aatccacagt	agaacacagt	51000
tgaacaccat	acaaggtaag	tattgtcatc	cttattttac	catgaggaaa	ttgatgctta	51060
gagagcataa	agccttggcc	aggggcacat	agttgggaag	ccgggggctaa	ttcatgcttg	51120
ggctctttct	gatagttttc	cttttttaat	tgtccctccc	tcattgttac	cttggggatt	51180
tcaagagatt	catgtagctt	ctaaatcaac	gaactgattc	ctggagagca	gcttctgtat	51240
gagaaaaaat	tagctaatta	tttatttcag	tgtctctgga	atgcaagctc	tgtcctgagc	51300
cacttagaaa	acaatttggg	atgacaagca	tgtgtctcac	aatgctgctc	tgggtggtna	51360
tgctgtgctg	ccagttgtca	tctttgaaca	aactgatgca	gtgctgggtt	aactcttctc	51420
ctttttggag	taagaaactt	tggaggcctg	tgtccttcta	gaagtttgct	gagcaaatgg	51480
taaggaaaaag	aaatagggtcc	taaggcttga	ctatttcaga	gaatttcttg	atttattgga	51540
ctgtcaatga	atgaattgga	atacatagt	gtaggctgtc	ttttcttctc	agacactgca	51600
atttccctcca	atctcttgac	ttttctagaa	gttttaatcc	aagtccctgt	tgggtggtna	51660
gataaaaagg	tattgttcta	ctagagactg	accttggcat	ggagatctca	tttggactca	51720
cagattttcta	gtctagcgt	tgggtttgta	tccataacctc	gctactgcat	tcttagttcc	51780
ttctgtcct	tgttcctcat	gcccagtgct	ccacctacc	cttgccccta	ctcctctaga	51840
ggccacagt	attcactgag	ccatttcata	agcacagcta	ggagagttca	tggctaccaa	51900
gtgccagcag	ggccgaattt	tcacctgtgt	gtcctccctt	ccatttttca	tcttctgccc	51960
cctccccagc	tttaacttta	atataactac	ttgggactat	tccagcatta	aataagggtta	52020
actgctggat	gggtggctgg	gatacacaga	atgtagtatc	ccttggtcac	gagaagacct	52080
tcttgcccta	gcatggcaaa	cagtcctcca	aggaggcacc	tgtgacaccc	aacggagtag	52140
gggggagggtg	tggtcagggtg	caggtggaac	aaggccagaa	gtgtgcatat	gtgctgacca	52200
tgggagcctg	tttgtcggtt	tcacagttga	tgccctgagc	ctgccatagc	agacttggtt	52260
ctccatggga	tgctgttttc	tttccagaga	cacagcgcta	gggttgctct	cattacctga	52320
gagccagggtg	tcggtagcat	tttcttggtg	tttactcaca	ctcatctaag	gcacgttggtg	52380
gttttccaga	ttaggaaact	gctttattga	tggtgctttt	tttttttttt	tttgagacag	52440
agtctcgctc	tgctgccatg	ctggagtgtg	gtggcacaat	cttggtctac	tgcacctccg	52500
cctgccaggt	tcagcgattc	tcctgcctca	gcctcccaag	tagctgggac	tacagggtgcc	52560
tgccaccatg	cccagctaatt	ttttgtattt	ttagttagaga	cgggggtttca	ccgtattggc	52620
taggatggctc	tcgattttct	gacctcgtga	tccgcctgcc	tgggcctccc	aaagtgtctg	52680

gattataggg	ttgagccacc	acgcctggcc	gatgggtgctt	tttatcattt	gaaggactca	52740
gttggtataac	ccactgaaaa	ttagtatgta	aggaagttca	gggaatagta	taagtcactc	52800
caggcttgag	gcaaaattta	caaatgctgc	tgactttgta	tgtaagggga	ggcattttct	52860
tagaanaagn	agaggtaggt	ctctgggatt	ccagtatgcc	atttccatcc	tcagtgtttt	52920
tggccacctg	agagaggtct	attttcagaa	atgcattctt	cattcccaga	tgataacatc	52980
tatagaacta	aaatgattag	gaccataaca	cgtagctcct	agcctgctgt	cggaaacacct	53040
cccagagtc	tctttgtggg	tgaaccocaga	ggctggggagc	tgggtgactca	tgatccattg	53100
agaagcagtc	atgatgcaga	gctgtgtgtt	ggaggtctca	gctgagaggg	ctggattagc	53160
agtcctcatt	ggtgtatggc	tttgagca	taactgatgg	ctgtttcccc	tcctgtctta	53220
tctttcagtt	aatgaccagc	cacnggcgtc	cctgctgtga	gctctggccg	ctgccttcca	53280
gggctcccga	gccacacgct	gggggtgctg	gctgagggaa	catggcttgt	tggcctcagc	53340
tgagggtgct	gctgtggaag	aacctcactt	tcagaagaag	acaaacagta	agcttgggtt	53400
tttcagcagc	gggggggtct	ctcatttttt	ctttgtgggt	ttgagttggg	gattggagga	53460
gggggggag	gaagggaagc	gtgttgggtt	tcacacaggg	attgatggaa	tctggctctt	53520
atggacacag	ractgtgtgg	tcgggatatg	gcatgtggct	tatcatagag	ggcagatttg	53580
cagccaggta	gaaatagtag	ctttgggttg	tgctactgcc	caggcatgag	ttctgatccc	53640
taggacctgg	ctccgaatcg	ccccagagca	ccccactttt	tccttttgct	gcagccctgg	53700
gagccacctg	gctctccaaa	agccctaat	gggcccctgt	atttctggaa	gctgtgggtg	53760
aagtgtagtt	gtggccccac	tcttagagat	caatactggg	tatcttgggt	tcaatctgga	53820
ttctttcctt	caggcctgga	ggaatataat	aactgagact	tgttttattt	ctgcagaggg	53880
ttctaagcca	ttcacttccc	agatgggcca	ataatgcttt	gagtaatctg	gagatcatct	53940
ttaatgcgca	ggtgaatgga	actcttccac	agagggatgt	gagggctgta	gagcagagt	54000
aactnccctga	aactcagacg	tcagctcttt	gtctctctat	ctctgaacac	ccttcccttag	54060
agatcccatc	tctaggatgc	atcttctgtt	agttagtttc	taagtctctt	gttctctgtt	54120
tgcccttatt	tttttttctt	ggattctaat	ccagtatccc	cacttggctg	tcttaatgta	54180
gcttaacatg	tctgtaatca	aaatgatcat	ctttctgaga	ttcaaagggc	tataagggac	54240
tttgagagag	atttcattca	gttttccctca	aactagaata	atgcttgcac	tgctgtgtaa	54300
agaacaaaag	tgtcaaaagca	tccttttgtt	cactaaaattt	ccttttttat	tatagtgtta	54360
cttaaatatt	aggaagttaa	aagtaggtat	aaacttcntt	ataggctgtt	attatacaac	54420
tatatgaccc	atacatattt	acaaattaa	tgcagccaaa	attgcaaaat	caataccatt	54480
caaattaata	ccttaaatgt	ggtgaggcag	ctgttgttca	actgaaacca	aattataagt	54540
tgcattggcag	taaatgctat	catgctgatc	attttgagtt	tggccagctt	atatntatca	54600
tgtgctaattg	attgaattct	ccaccatttt	ttctacttgt	atgaccttaa	ttgtatggca	54660
cctgttccat	cctcatgagt	ttgctacaat	tatactgggt	ccaacacaa	cataaacaca	54720
aatataaact	tgggttttga	aatcttgtgc	cagaacttgg	cttttaaagta	agcattttaa	54780
aaatccatat	gtgtttatta	gactttgttt	agatgactgt	tgaatgaaa	acaaagtgtt	54840
taaaaatctc	ttagagaact	taaatataat	ccctcagcaa	tatgtataca	gatcttccct	54900
tgagaaaaac	tgattgtgtt	cagcctctca	tgttacaaat	ggggaacctg	aattctgagg	54960
tctctagtga	gagaacaggg	actggaatct	gtggantcct	atctgtttta	ataataattg	55020
taaagtataa	tagataaat	tatattata	aaataaaagc	aaacacttag	aatgagcttc	55080
catgtgtgag	gcactaactg	attaggcatt	attaactaga	tttattcctt	taaaggcccc	55140
gcgatgtact	gttatttcca	catgtttag	ctggggaacg	tgctactcag	agaggttaag	55200
taacttgtct	gaggtccaca	ccactaaca	ggagcacagg	taggggtcaa	atccagataa	55260
tctgactttg	gagctggcac	tctaactcaa	tgtgccta	cgcttttcag	tgggtgtcatt	55320
attttgccta	ttctccatct	gagaatattg	aagtttctga	ctccttccct	gcctttctcc	55380
ctgcctcccg	tgggttatccc	caggtcctgg	tgttccagtc	ctctatgtcc	gtccttactc	55440
ttattccttt	gctacagtgt	gatccagggc	tcctgcccct	tcttatcctg	gtagaggggg	55500
cccacttgc	gggaaattgt	ctccgccatg	gtttatccat	gttggtgtgc	cattagttag	55560
tagtgggaag	aatcatatca	tggtggcaat	gaaagggggg	ctatggctct	ggggtagtct	55620
agtcgtgaac	tcttatttta	cggatgagaa	agctgaggt	caaagcaggg	aagggatttc	55680
ttgaggtcac	ccagccagca	actgagctgc	aaccagaagc	tgagatcccc	aggactaggg	55740
ccgagcctca	ttctgtccca	tcacagtgc	ttttcttccc	tcctccaaac	tatttttatt	55800
ttttattttt	ttgcagctgc	ttagcagctt	gaagttagaa	gaaagggcag	ggaaaagggt	55860
ttccgtgctt	agccagggaa	ggaatcctgc	aacaggatgt	gggggtgggt	cattcaaatt	55920

```

gggccagact ccactgggtct tgttgccttct tgcttggtat tgcagatggg tttaaaagtg 55980
ttaggattag agagataggc aggttttagcc aaaggcagtt tgtagccttg tggcagagtt 56040
ctttttaaag aaggaagtgg gatgcaacac cctgacacaa aggggcttaa gttgttatac 56100
cactgcctgc taacctgttt tccttaacte tcttccctgat ttctaaagga agtatatttt 56160
gctgaatcag aaagaaaagt gatttatttc aggttgctga tgcttagatt gttagagttg 56220
gaaagatctg gcttgcctct tgtacagctg acagaactgg ggctcagggg ggcacaggtg 56280
cccagagttg gtcagtcagg aaagtagcac cagaaccagt ctccctggtg ccctacagtt 56340
gcagaccctt ttttgctttg ctctctgtgt atactaaagc ttctatgtct ctgaatctca 56400
agttctgact ggtagctact ttccaatcca cctggcttag atttctagat tatattgttt 56460
agacgtcaga acctcttaag ggttttgggg ccacttgtaa gctcacatag tgagaaccag 56520
ccctgccccat taggtagggg aagaagttag cagtccatga tagctgttgc ctgcagcgta 56580
tggatgttca ttgcacagtt cctgtctcct gatgcctgg agtgatacag cttggcctca 56640
gagcccagca cagagcctgg cccttggggac atgcttagta agtatttact gaatgagttg 56700
gaaatgtctt aaggcccat agtttgacag tcttgaggag gctcccttgc actaggaaga 56760
atagaaaagca tacataaagc ctgtgtgctg ccgccaggaa gactagaaac gctatgttca 56820
gcctggagct gaatggtata ccccagagca accctgttga aaggcagtg cttgccttttc 56880
attctgtgtc ctgggttgct ggtaactcct ggggtccctg cctctcctgt accccattg 56940
tgcagactga gggggggacca tcagccaggg ttagttttcc gctgtttctg ttaggcaag 57000
aataaaattga attgagttgt gaaagtggg tgcaaaagctc agtttgggtc caaagtaaca 57060
gttaacttgt gtgggtggca ggtattcagt acaaacaggg ctggggacag gaaggggaag 57120
agaacttcag agctttcacg atcctcatct ggttttaggc tgatccagag gccaaagtcc 57180
ccatggaaca aactggacaa agtgaggggtg gccacatggc ctcttttctt ttgcctttat 57240
tattaatttt ctcaaataga tctgactagt catgtggctg ggaaaatagt taattgtgat 57300
tttttttttt ttaactgag tctcactcta ttgccaggc tggagtgcag tggatgatc 57360
tcagctcgcc gcaacctctg cctcccgga tcaagcaatt gtcatgcctc agcctcccg 57420
gtagctggga ttatgggcac acagcaccac gcctggctaa tttttgtatt ttagtagag 57480
acatggtttt agcatgttgg ccaggtggt ctgaaactcc tgacctcaag tgatccacc 57540
acctcagcct tocaatctgc tgggattaca ggcattgagcc actgcaccca gccagagtac 57600
cactatttgg gcattcttta atgaaaaaga atgaactatc caaaaattaa aactcctcat 57660
ttatgagctt ttagagaatt ttacagagta gatggaaact ctctgcaccc tttccccact 57720
tctagtttca cctgacacat ttcttccctg tcttactcc tgggccggca gcagtggtca 57780
tgattccaat cccagcttgg ccaccatctg cctcagtggc ctaggaaaac tcctttctcc 57840
agagctttag tttctcttc tacggaatga agaaaagttaa aacaaataga catttattgt 57900
ttcatttggg taaatatcta ttaagcatct attacttgtg gtatgggttag ctgggtatat 57960
agtgggtgaag cagctgggca tgagtactgc tttcgtagag cttacagttc agtgaggcca 58020
gcagatgtga aacatatcat cacacaaata aaaaataaac tatcaactgt gatgaggatt 58080
atgaaggaaa aaatccggca aactatggta cctgtgttag atactagcag gtgtgggttag 58140
ggatttcatt tagattgaca ggttgtcaca ttaaagctga gagccctgaa gttcaagcaa 58200
tgggttagcca ggcaaagatc agaggcttag agataggga atccattcca ggcagagaga 58260
ctgggggtgc ctgtccccta ggtcaggga cagaagaaag ccagtggcac tgggtggagt 58320
aataagactg gggggggatg agttggtagt agacatgacc agatmattta gggcncaatt 58380
ctcncgtggg naaggagaat tntaatttaa ttttatttta ttttatttta 58440
tttatttatt ttttattttt tcaagacgga gtctagttct gtcgccagg ctggagtga 58500
gtggagcaat ctgggtcac tgcaactttt gcctcctggg ttcaagcgat tctnccctgc 58560
tcagnccctc tagtagctgg gattacagac gccaccacc atgccagct aantttttgt 58620
atttttatag agatgcgggt tcaccatatt ggcaggctg gtctgaaact cctgaccttg 58680
tgatccctct acctcggtt cccaaagtgc tgggattaca ggcgtgacct acagtcccc 58740
ctgagaattt aattttattt tatgtgcaag aggattccct gaggtagtca ggccacattg 58800
tctgggtgact cttgggtag agggaaactt aatgacaaag gcccaagaaa gcaattgtaa 58860
tcattacata tacatggacc attttatgtt gttttcttct ttcatttaac attatttagt 58920
gtgctgttct acatatttct aaatcatctt ctgattttaga ataattgatt ctgatgtga 58980
ggctgtgttt tatagttttg aaagtaatac tttgatatcc attacttntc ttgattctca 59040
cagcaattct gnaggtgtat gcgttgcaat ttctgtttca cagatgaaga gagtattgtt 59100
aataagttaa tggccgggca tgggtggctca cacctataat tccagcactt tgggagacca 59160

```

agggtgggagg	atcacttgag	gccaggaatt	tgagaccagc	ctgggtcaatg	tggtgacacc	59220
catctctact	aaaaatacaa	aaattagcca	ggcgtggtag	cacttgccctg	taatcccagc	59280
tatttgggag	gggtgaggcag	gagaatttgc	ttgaacctgg	cagggtggaag	ttgcagtgag	59340
ccaagattgc	accactgtac	tccctgctgg	gtgacagagc	gagactctgt	ctcaaaaaat	59400
aaaaagttgc	taagaggagg	gctgggatct	tttggctcca	aatctactgt	gggatgatgc	59460
ctttgacatt	cctgatagct	gtgcagtaat	ccattaacac	agtttttata	agttcaaan	59520
cctgttgcca	acatttagat	tggtccatgt	gtgctgttac	aaataaatta	ctataaagat	59580
tctatacatt	taatctttta	ttatttttgt	attatttctg	tagggcaaaa	tctgaggaac	59640
aggattacta	gggtgaagg	aaatggccct	tgaagtgtct	gatcagatgt	ctttccagag	59700
gatccaacca	atttaaatag	ccaccatcaa	tgcatgagac	ttttagtttc	aggggaaggca	59760
ggcctgggtt	taaaaatcat	ttccctctct	tagcattttt	ctgatgtgat	ccttaagatt	59820
tcactttagt	tttcccaggt	ctcattggca	tgtatgctgt	tagggatggg	tctaaaaatta	59880
atttttcttc	acattcatat	catgtcatcc	cagtgtattat	ttataaata	atcattgtat	59940
taaatagtga	ttccttttct	agttattttt	gggacattta	ttaaaacctg	gatattggtg	60000
ctcatgcttg	tattcccagc	actttgggag	gctgagggtg	ggggattgct	tgagactagg	60060
agttcaacac	cagcctgggc	agcatagcaa	gactccatct	ctataaaaaat	aaggaaatta	60120
gtcaggcatg	gtnggtactt	gcctggagtc	ccagctactt	ggaaggctga	ggtaggagaa	60180
ttgcttgagt	ccagggtggtc	aaggctgcag	tgagctatga	ccatactact	gtactccagc	60240
ctgggcaaca	gagtgaacct	ctgtctgaaa	aaaaaaaaaa	aaaaaaaaaa	aaannnnnnn	60300
aaaaaaaaaga	tgtgtaggga	gcaatttttg	agttattcat	ttgggtcattt	gatattgtat	60360
tttagttttg	gtgctgatag	agcccagaat	gtaccctgaa	tttgatgaac	attctgatat	60420
atgggggagc	tcattgtccc	ccacttacct	ttttgcctct	cagaatatct	tttgatatct	60480
ttatctgttt	tttcccatt	gaatgttatt	accttatcaa	gctcaaaaaa	gtaccctatc	60540
gctattttta	gttcagttgt	gttaaatcta	taaattagct	tgggaaattt	ggatattaaa	60600
tgaactcatg	aagaagcaga	gtttagctct	ccttaattct	catcttccct	tatttatcct	60660
actacagttc	tgtgggtttc	ttttatgtaa	gaagcacatg	ntttggctaa	gttaatgcct	60720
agggtttttt	gtttatgtgt	ccattctcac	tgtggatagt	attctctttt	ccccacatta	60780
tattaattta	actggttttc	agagactaat	agcaatgcta	ttatttagga	gaatttacct	60840
tggttctgat	taacttacc	atacttgcaa	atcatttgca	gctttttagt	taactttgtg	60900
agttctctta	gatttacgac	catgccagaa	acagaaagga	tattttcatc	tcttcttttc	60960
tgatgtttat	tcttcttggt	tccttttttt	atcccccat	atattctcaa	gaatctctca	61020
atacaagaa	atagcgactt	catttttcag	cgnccggagt	cattattttg	gctaccatga	61080
ttcagaagcc	tcttgccctaa	ggcccaattt	tattctgcta	gttttctctg	ttctttgtac	61140
atggcccttg	cgtgcctcta	accttgaatt	aacgtggcta	aatctcaaga	atttaagagc	61200
accgtgactg	tgtcctcagg	ctagggagg	aaatgggttc	acagagtga	tggattgtgg	61260
tctatgaact	tcggcagcca	gcagcaaaag	tcaggcatga	ataatcaagt	ggacagtga	61320
catctgtagt	gtgggagatg	ttggcataac	tatgaatgat	gattcaagag	tggtttgatg	61380
catattgaat	aacatgatga	taagtactag	actctgtgct	aagccttcta	tgtgaaatac	61440
atttaattct	cataataact	ctagagcagt	ggttctcgac	cggggccggt	tatcccccta	61500
ccccacccta	ccctcaccct	tccaccagg	acataacatc	tggagatatt	tttggttgtc	61560
acaatcctgg	gaatgtatgt	gctgatattt	agaggttgag	gtcagggatg	ctgctgaact	61620
tcgtagaatt	cataggagag	tctctcacia	cacctatctg	gccccaaatg	tcagtagggt	61680
cactatcaag	aaaatctgct	ctagcagtgc	ctgctcatat	tatccccatg	ttgaaatagc	61740
aagatgggaa	gtgcaaagtg	gtgcttcggt	actcttggag	cagctttgac	tttggttgaga	61800
aacgcctttt	aaaaacaatg	tttcttccca	tcttcccacc	ccatggggag	gtgtgggggt	61860
gggtgggtag	gcaccaaagc	aagatttaga	agagttttct	gtaggaattt	ataatggtaa	61920
aggatcaact	tcatttccaa	gctatttatg	agggtttatg	tttaggaaaa	gtgctaagct	61980
tagagaagga	ggagaaatct	gattttatta	atgagtgtag	ccataatggc	atatcctggc	62040
agaagtcaac	tttggtttct	agagggaggc	tattatgaaa	agaaatacct	ggaacattcc	62100
cctgggtttg	gaaggtgagt	tctaggttca	atgatgggaa	gaattttaga	ggtccaagat	62160
aaaaggggcaa	agattaaatt	ttgtctctca	tgagttctct	ggctcagggt	gtgtgaactt	62220
tgacagcagt	ctctttaatt	cactcataca	tgctagtctc	ccagctcagc	aagggtcttg	62280
agagagcagg	tgtctgtatg	ctctggtaag	tgaaggcaaa	gtgcataagg	agggtgggg	62340
ccataatggc	gaagagaagg	agcccttcag	tcagagtggc	tttgaatctt	ggctctgcca	62400

tttgccaatc	ttggaccatt	gggcagtgtg	ttaaactcttt	gaatctcagc	ttcctcttct	62460
gtaaaatgtg	tataacaaga	gtactaattg	gattgtttga	tgattaaaatg	agttaatgtg	62520
tataaagcac	tcacaaccct	ggtacatagt	aagacctttc	attattatta	tcacatcaaa	62580
ttttttttta	cctcttttcc	tgatctgctt	acactcacca	gcttcagctg	ctccaaatgg	62640
cttgtaagat	tttttgtttg	ccctttgctg	tcagttgcca	tggggaagat	ccattcattt	62700
ttttcagtca	accaacatat	tttgagcatc	tgctgcccta	caggatccta	gatatggggg	62760
ctgcagagat	atccaggaac	ataagccttg	attaattggg	tcagatcagt	gctcagcagg	62820
gctggcaagt	gctagggtttc	ttttaagtgg	catatcttaa	aaggatatatg	tcctnaaaca	62880
tagctttgtg	atggcagcat	gatgggtaca	aaagcacaca	cttaagtgtc	agtagatctg	62940
ggttcaaaca	ttggtgcagt	ttcttatggc	tcgtaacttg	ttcaaaccctc	agttttcttca	63000
cttctaaaac	ggtaatgata	caacctacct	cacagggtta	ttatgaatta	aatactggag	63060
atgagatata	caaaacgtct	tgagntacac	agtagctgcc	caatattggc	tgtaagtatt	63120
ataaatctac	aagctgtgaa	ttaattttac	ctctctggat	cctgnttgat	atttctagac	63180
cattccacct	agtggggcca	tttccctacc	gagtcaccgg	tggtgtcaaa	tagaatgtca	63240
tgtggcctcc	tgagttgggt	agaattggct	gctcatctca	accccgctac	tgactatctc	63300
tgtgatttac	ccttccctcca	gccttagcct	tgctacatat	aaaatcaaga	caataatggt	63360
tcctatctca	caggggttgtc	ctgaggatta	aattaagtta	ttaatataaa	atgtgccttg	63420
tacatattgg	gccttaaata	aacagtagct	actattttatc	cttaaagtac	aaatggtagt	63480
ttcagagcct	caaggctgat	ggctattttat	cttactcata	ctctttgttt	agcttcattt	63540
ttttccctta	atttcattag	wattttcttt	tctctttttt	tttttttttt	tttttttttt	63600
ttttgaggtg	aagtctcact	ctggtgcccc	ggctggagtg	caatggagcg	atcttggtctc	63660
accccaacct	ctgtctcctg	ggttcaaaaca	gttctcctgc	ctcagcctcc	cgagtagctg	63720
ggattacagg	ctcccgccac	catgcccagg	tatttttttg	tattttcagt	agagatgggg	63780
tttcaccctt	ttgaccagge	tggtcttgaa	ctcctgacct	catgatcaac	ccacctcagc	63840
ctcccaaagt	gctgggatta	cagggtgtgag	ccaccacgcc	cggcctcata	agtattttct	63900
aaattttatt	acagtcatgc	cattttaaaag	gaaagtgtga	ttcctgtctt	tgttaatat	63960
tataagtgat	tttattcagc	tacaagcttg	gaatggcata	taatttttga	ttctgctttt	64020
ttcacttaat	attacatggc	taatgatttc	tgtgtttcat	aaacattatt	ctgatgatgg	64080
catgatatat	tgttgagtac	atgtaccata	attgaatcat	ttccctattg	ctatgcaatt	64140
aagttgtttc	caatattttg	caattataat	gtttcaatga	atgaataact	ttatgcatat	64200
agctttttga	tatcttaagt	tcagtttctt	aggatgaatt	tccaggaata	gtaattgggc	64260
aaatgggata	aacatgactc	ttgaatacgt	attgttaaca	ttgctttccc	aaagggctca	64320
actgatttat	atttcogtgt	tcattatctt	ttaaaccagg	tcatttactc	accaaacatt	64380
tttaaagcca	ttatcatgtg	gtaggcttag	taagaagaaa	gtgaccctaa	gggagaagct	64440
tatatataaa	tagggtccct	ggtgtacca	gtgctgatac	agacacaaag	tacctggggg	64500
aattgagatg	agggagtcc	ggctcagctg	ggagaaaaagt	tcattttcat	agagtcattg	64560
ttttgttctt	tggcagaaa	aaaattgctt	tcttccccac	ccccaccccc	agctttattg	64620
aggtataatt	gacaaataaa	aattgtatat	ctttaagata	tgcaatgtga	tatatatgta	64680
tatctcaact	taaaaaataa	gctacagaat	aaaaaggtgt	ttgctattaa	aaaaaaagaa	64740
aaggctgaat	gtcattccca	agcttggaag	tttgagtatg	ttgcctcttt	gggattattt	64800
acagaaatat	tagcaagacc	agccccatct	ttggctctga	gtactccact	gtcagcatgc	64860
tttcttccag	agagggatcc	atttgccctt	atttttcatt	ctggttggtcc	gtctatgcaa	64920
actattcttg	atagttttat	ggtaacagtg	tttttttggt	ccatgagatn	aatttatata	64980
tgctcattgt	ggaaaattta	gaaaagacag	gaaagtatta	aaanacatca	cttttttttt	65040
tttttttttt	tttttttttt	taagnagaca	gagtcctgct	ctgtcgcccc	ggccggagtg	65100
cagtggcggt	atctcagctc	acagcaacct	ccgcttcccc	ggtttaagtg	attctcctgc	65160
ctcagcctcc	caagtagctg	ggagtacagg	catgcaccac	cacgcccggc	taatttttga	65220
tttttagtag	agatgggggt	tcaccatggt	ggccaggctg	gtctcaaact	cctgacctca	65280
ggtgatccgc	ctgccttggc	ctcgcaaagt	tctgggatta	taggcaggag	ccactgctgc	65340
agccacacct	acgttcttat	catcctagta	catccactgt	cattatcttg	ctgtatttcc	65400
ttctgcccag	tctcactctg	atcatgcagt	ggcgtgatca	tgcaagtatc	tcggctcact	65460
gcaacctagg	ccttctgggt	tcgagtatt	ctcctgcctt	agcctcctgg	gttcaagtga	65520
ttctcttgcc	ttggcctccc	aagtagctgg	gattacaggg	atacaccccc	atgcccatct	65580
aatttttgta	tttttagtag	acacagcgtt	tcactaaaat	tttgtatttt	tagtagagat	65640

ggggtttcac	catgttggcc	aggctggctc	ccaactcctg	acctcaggtg	atccgcctgc	65700
cttggcctca	caaagtgatt	acaggcatga	gccactgcat	ccatcgccaa	aaagattttt	65760
taaaagagtt	taatgtagaa	ccatatcaaa	ggctcttggg	aataaaaaac	agttttttta	65820
aaatatcaga	aataaaaaca	caaataaata	aataaaataa	aacacccaaa	acaatctgaa	65880
gcacgagcac	ctagcagaaa	ggttcaatta	tgatctattc	atagagtggg	atatcaagta	65940
gacattacag	gacatgtttt	aagattatat	tttatgtcat	gggaaatgct	ctcccagtat	66000
gatgttaa	gaaaaaacag	aatacaaaa	tatatatgct	gcatagtctc	aatattgtag	66060
agaaaaata	ttatttatgt	atgcatgaaa	aaagacaaaa	gatgttaaca	gagatccatt	66120
gttacttcag	tttactaggg	attgtctctg	ggaggttagg	ttaagggtgat	ttatatattac	66180
ctttttaaac	ttttctgtat	ttttttattt	tcaaattttc	cataaaaata	taaggacttg	66240
aagatcaaga	aaaaatttct	gctttggctc	agtgcagtgg	ctcacgcctg	taatcccagc	66300
agtttgggag	ccctagggga	gaggatcact	tgaacccaag	agtttgacgt	tccagtgagc	66360
tatgatctcc	ggatcgtacc	gcctggacga	tggagcaaga	ccctgtctca	aaaaaaaaaa	66420
tctttgcttt	ttttttttgt	ttgtttttga	gacggagtct	ctctctgttg	ccccagctgg	66480
agtacagtgg	cacaatctca	gctcaccgca	acctctgcct	cctgggttca	agcgattctc	66540
ttgcctcagc	ctcccaagta	cctgggattc	catgcaccca	ccactatgcc	cagctacttt	66600
tttgatattt	cagtagagac	agggtttcac	catgttggcc	aggctggtct	cgaattcctg	66660
acctcagctg	atccaccggc	cttggcctcc	caaagtgtct	ggattacagg	catgagccac	66720
tgtgcccagc	ccaatctttt	gcttttttta	aaaaaagaag	acaaaaagg	attttatacc	66780
agtattatct	tggtgtgtgt	actctgaagc	cacagttgta	agttataatt	actctgaaac	66840
acaaggccct	gtgactcttt	tgggctcttt	ggtgtttatc	ttgattacaa	cgttggaata	66900
tagaaatgaa	aggaatggga	gaggtgatag	acttcaggca	gtgtaactag	ttgtctgaac	66960
actactggct	caattatatt	gtgtctagt	atttccatct	tgtccgtctg	ctaattttatc	67020
gcctggtaac	tcactgaggc	agggttttcc	tttggagaaa	cctcattgtt	ttaaccagtg	67080
tatcatgctt	gtttagaagt	tcaatgatct	ttttaactca	tgggagaaga	tgatgaccag	67140
acctggacag	atgggggaag	actttgcact	ctctctttac	agtcctgagt	gcacacaggt	67200
caatatggaa	ctatgtgtga	attttcattg	tctttgagag	ccctcttctc	tgccccatag	67260
ggagcagctt	tgtgtgcaat	tagaggagca	agggttgtgt	gtatttagca	cagcaggttg	67320
gcctggctct	ctcctctcaa	catagtcacc	acataacctg	cactatgcta	aggctgggaa	67380
tgcagacaga	tgggtgcctg	ctttcagagt	gctcaatgtg	ctgaggaagc	cagcaacaga	67440
aacagatgat	ttcaggagct	ccaggaaaat	gctacaggag	gagtggtcct	gggttactgg	67500
agtagcacag	gaggagggct	tctagctcag	gctgagattt	tagtaaagga	aattatgcca	67560
cgttggtaac	taagaatga	atagaagtga	accagataaa	gcacgatagg	aagcatcttc	67620
cttaacctaa	gggaagacac	agaggtatat	ggaatgggat	gttaaaaggt	tgggactcca	67680
aacagttctg	ttaaagctta	gagagtgggt	ggagagactg	gagaagttga	ttatttagta	67740
aatgaagtgt	tctgtggatt	tcccagatcc	cagtggcatt	ggatatccat	attattttta	67800
aattttacagt	gttctatctt	atttcccact	cagtgtcagc	tgctgctgga	agtggcctgg	67860
cctctattta	tcttctgat	cctgatctct	gttcggctga	gctacccacc	ctatgaacaa	67920
catgaatgta	agtaactgtg	gatgttgctt	gagactcacc	aatggcaggg	aaaatccagg	67980
caattaacgt	gggctaaaat	ggacttttcc	aaagatgctg	tctttgggaa	acatcacaca	68040
tgctttggat	cagnaaaacc	taggcttcta	atttggtgat	aaggcatgaa	ctcaggagac	68100
tgttttcagt	cctagtgaat	ggtgataatt	gtaattataa	cagtagacaa	catctctttt	68160
acacatttta	aatcatgaaa	atagaataac	cttactgata	attttagaaa	gtgggtgatta	68220
aaagcacatt	taagataatg	ccttaacacc	tagtcttttc	catatgcatg	atgtcttaat	68280
cacacattgc	aaatcatgga	acacagaatt	ttaagcagca	tttgtgtaga	acttctcagt	68340
tttactaata	ttattttatt	ttattctcat	aacaaccttg	aatagaactc	agatcatctg	68400
tcaatcatgt	attttgataa	cagcctttac	agtgagcata	gaaaatacag	tagtggctaa	68460
caacacaggc	tccagatgtc	aggttatctg	ggtatgaatt	ctgggtgtcag	cattcactaa	68520
gcatatgacc	ttggacaagt	gatttaagtt	tcttttaaac	agagaatagt	aatacctacc	68580
tcatattatt	attgtcagtg	tatcatctta	caatcacagt	ctttctctta	gggctgggct	68640
cagtgggtgg	attgacactg	cagaaatggc	gagatctaaa	ggatcaacat	ttacgtagct	68700
gggaaatgta	gctgggactt	cagtttctac	gccctagtga	tttttcttac	cactaagcag	68760
ctcagtcctat	acccctacga	gacccacaag	cttatgagat	actgttcttc	caggaaagca	68820
gtggggccag	ggccaccttt	taattgtgtt	tcttggcctg	gtcccatctt	tctcacaata	68880

tatagcaaca	gttattttact	tgctgatttt	ctaattgcaca	tcacacatag	tcatattaaa	68940
cacacacaca	cacacacaca	cacacacaca	cccccaaga	aacattttct	gagacgtgat	69000
ttcctgattt	catcaaaaaa	gaaaagagcg	ggccaggcac	agtgggaagt	caaggtgggt	69060
ggatcacttg	aggtcaggag	tttgaaacca	gcctggccaa	cacggtggaa	cctcgtctct	69120
actaaaaata	caaaaattag	ccaggcgtgg	tgggcgacac	ctgtaatccc	agctactggg	69180
gaggctgagg	caggagaatt	gcttcaacct	gcgaggctga	gggtgcagt	agccgagatt	69240
gcgccattgc	actccagcct	gggcaacaga	gtgagactct	gtctcaaaaa	aaaaaaaaaa	69300
aaaaaaagca	taaactgaaa	tttatatgca	atztatatgc	ctgtgagata	attctgtttt	69360
ctcttttggg	accccaaaga	gatttttttg	attgatgagc	aaatacattt	tagattttat	69420
ttaaagcatta	tgccaagcac	caactgaagta	taagtttcaa	gggcaaacct	agttttttca	69480
tctactagac	gaatgatttt	ctggaatgat	tacaagcagg	caangatggg	gnntagtgga	69540
aatagcaaat	gtcttcggca	tcagacaagt	tggggtttgt	ttgtatcctg	cctctgccct	69600
tcaccgaggt	tgtgatcttg	ggcagattgt	tgagttttta	cctagattcc	tctgactcca	69660
gatcataaat	tttcagaaaa	gttctgaaat	tcttgtatat	actgatggta	aatgagactt	69720
ttcctttacat	ctatgcactt	ctttgtttgt	ttgttttgag	atgggtctgc	tctgttgccc	69780
agactggagt	gcagtagtgc	aatctccgct	cactacaatg	tctgcctccc	aggttccagt	69840
gagcctcctg	cctcagcctc	ccaaatagct	gagactacag	gcatgtgcc	ccacgtccgg	69900
ctaatttttg	tatttttagt	agagacaggg	ttttgccatg	ttgaccacac	tggtctcgaa	69960
ctcctggcct	caggtgattc	gccgcctca	gcctcccaaa	gtgctgggat	tacaggcatg	70020
agcccgacatg	cccgccata	tccatgcact	tcttgcaacc	ttaccttctt	ttctcatcac	70080
cctccaggga	cctagtggga	agagcagagt	taaaagttaa	ggtgaaactt	ggagaggtgt	70140
cttgtcccta	ggaacaaagg	actgggttga	aattctctgt	aaatcttccc	cagttcaaac	70200
cagagttatc	aaggtcttaa	aaacttccct	gggtcctgag	agccatttat	attatttact	70260
tgtcttccctg	tacacccact	gcctagtccct	gacccctactt	ttgtttgcaa	ataggatggg	70320
gcacaacgta	caaggaaggg	cctttgccac	ccctgctaag	ggataacctg	aaataccttc	70380
accatcactg	ccctgtgctg	cttttcacct	atgccagtct	gtctacagt	ccagtgtctc	70440
ctggcattga	aagggggagaa	tcttttggtc	ctttgagtat	ttgggtgggt	tacataaatc	70500
tccctgaatg	aagagcagct	gacttaggca	aggggccttg	tttggttttc	cttgaactat	70560
taacaggaag	ataggggagat	taactgtgta	aatgttcaat	aggccagagt	ccctgcagag	70620
gggtggccaca	gtgatcagat	cttatcacat	ccttgctttg	ggtgttgccct	ctctgggttg	70680
agtatggata	gaaaagaaa	aaagacccta	tattgaaatg	caaagtgcag	caagtccctga	70740
ctttggatta	acttctcagc	ccatttgcct	gaaaataaaa	agatgaataa	aacaagggtc	70800
ccactttgga	gggaggtggg	agctgtgaga	gttcctgctg	ggtcctgctg	ggcaacagca	70860
gagtaagtgc	tggggttagat	tcactcccac	agtgcctgga	aaatcctcat	aggctcattt	70920
gttgagtctt	tgtcctacac	caggcactct	gcaaaaaacgc	tttgccctgca	aggctctcatg	70980
cgatgctcac	cacagctctg	tgaagttaat	tgtactttta	tcaccatttt	acagatgaga	71040
aaactgaggg	tatgggggtca	atgacttggc	taaaagtcact	gcttagcaag	ctgcagggac	71100
tggaatgtgaa	ttccaattgg	tttgactcca	aagcctgtga	agctacttgt	tcttcaccac	71160
ctagagctgt	ggttcttgat	aactgtgaac	tcttttgggg	tcacaaatag	ccctgagaat	71220
atgatagaag	caggagctct	ggcctttctg	tccatacctg	aacaggctct	tggtgtaaga	71280
gccccctcgtc	cagggcctat	taatcttgat	cctcataagc	agcatccatg	tattacgggc	71340
gcaaaaccaa	ctgtgccaga	ccgaatccta	ggaccaagcc	caaataatgtc	ccatcatcct	71400
tttggttaaga	agctcattgt	aagaaagaaa	gaggagagca	agaggatgac	ctagtgcattg	71460
gggcctcatt	gttttaatta	gtgacaaaac	aacaataata	acaacaaaac	ccccgaagct	71520
tcacagatga	catcagaccc	caagcctgtg	tgtttttcag	gtgcccttga	ggagctttgt	71580
agctggcaga	ggaggtgaaa	ctgacaaatg	tttggcagat	ggaggagagt	accagagggg	71640
tttgagatga	gctaaattcc	aatctaaccg	caggtgtgag	gaagaggctt	ggattggggac	71700
catggagatg	gggttcttac	tcccagtcac	gccagctgac	tttgcgagt	ttctttgtca	71760
gtcactttat	cttattttat	ttatttttat	ttttttgaaa	tggaagtttcg	ctcttgtcgc	71820
ccaggctgga	gtgaaatggc	gcgatcttgg	ctcactgcaa	cctccccctc	ctgagttcaa	71880
gcgattctcc	tgccctcagcc	tccagagtac	ctgggattac	aggcgccctg	caccaagccc	71940
atcgaaatttt	tgtatgctta	gtagagacag	ggttttcgcca	tggtggccag	ggtggtcttg	72000
aactcctgac	ctcaggtgat	ccgcccacct	tggcctccca	aagtgtctggg	attacaggcg	72060
cgagccactg	tgcccagccc	acttcatctt	accgtagtta	cctccttaga	gtatgaaaaa	72120

ataggcttag	ggcatcccca	agteccctct	atgtctgaga	gctgaggctg	gctgtcaaa	72180
aggaactaag	gatgccaggg	actttctgct	taggaccct	ctcatcactt	ctccaacgct	72240
ggtatcatga	acccattct	acagatgatg	tccactagat	taagaatggc	atgtgaggcc	72300
aagtttccac	ctgagagtca	gttttattca	gaagagacag	gtctctggga	tgtggggaat	72360
gggacggaca	gacttggcat	gaagcattgt	ataaatggag	cctcaaaatc	gcttcaggga	72420
attaattgtt	ctccctgtgt	ttttctactc	ctcgatttca	acaggccatt	ttccaaataa	72480
agccatgccc	tctgcaggaa	cacttccttg	ggttcagggg	attatctgta	atgccaacaa	72540
cccctgtttc	cgttacccga	ctcctgggga	ggctcccggg	gttgttgga	actttaacaa	72600
atccatgtaa	gtatcagatc	aggttttctt	tccaaacttg	tcagttaatc	cttttccctc	72660
ctttcttgte	ctctggagaa	ttttgaatgg	ctggatttaa	gtgaagtgt	ttttgtaaat	72720
gcttgtgtga	tagagtctgc	agaatgaggg	aagggagaat	tttgagaaat	ttggggtatt	72780
tggggtatcc	atcacctoga	gtattttatca	tttctgtatg	ttgtgaacat	ttcaagtcct	72840
gtctgctagc	tatttttgaa	tatactatat	gttgtaaatg	atatcatgca	gcagacgtgc	72900
atctgaatgg	gctggctcta	ggagctagag	ggtaggggct	ggcacaaga	tgcatgctgg	72960
aagggtcctt	gcccataaga	agctgacagc	caaggctagg	ggagttctgt	cttctctgca	73020
tcaggtcacc	tctctcacct	ctgtcactgc	cccatcagac	tacaatgtct	gcaggtcttt	73080
ctcccctgag	tgtgagctcc	ctgagcaaa	caggatgctg	ccccttccct	ttgtattcct	73140
ggctcctggc	ttcagtgcct	ggacataagt	atgggcataa	taagtgtccc	ccaaatgaga	73200
cattgaggat	tcttcaaata	cacaggaccg	tgatgtgagt	taggacggag	taaggcagat	73260
gggatgtggc	tcaggacaat	cctgaggaag	ctgcagctgc	ggcacgcagg	gccacactgt	73320
catgttcatg	gaccctagac	tggctttgta	gcctccatgg	gccccttcca	tacacaaata	73380
ttaaaaatta	tatttcatga	ctgncattgg	tataaagatg	aatataatcc	agaccagatt	73440
catgattatt	catacatttt	tagtgtatta	acttttaatt	ctgcttttaa	aataaaattaa	73500
aacattctaa	tatgccctta	agagtatccc	aggcccaggc	cactgagcct	actgtggttc	73560
atggataagn	ttggccctgg	gggcatgtgt	gtgcatgcat	gtgtgtgcac	atgcatgatg	73620
agccgggcct	tgaagggtgg	taagatttgg	gtgtgtagac	caatggagaa	aggcatttgg	73680
ggcagtgatg	atgggtgggg	gagggaaat	ggtgatgaat	ggagctgggt	gtggggagcc	73740
atgggagtgg	gttagggcca	gcctgtggag	gacctgggag	ccaggctgag	ttctatgcac	73800
ttggcagtca	cttctgtaaa	gcagcagagg	cagttggcct	agctaaagcc	tttcgccttt	73860
tcttgacccc	tttacagtgt	ggctcgcctg	ttctcagatg	ctcggaggct	tcttttatac	73920
agccagaaa	acaccagcat	gaaggacatg	cgcaaaagtc	tgagaacatt	acagcagatc	73980
aagaaatcca	gctcaagtaa	gtaaaaacct	tctctgcac	cgtttataat	tggaaattga	74040
cctgcaccag	ggaaaagagag	tagcccaggt	gtctggggct	tgttcccat	agatcttccc	74100
caaggggttt	ttctccttgg	tggctggcct	gtggggcccc	tctccaggag	gcattggtga	74160
agaaactagg	ggagctgggt	gccacagaca	gtgatgtact	aatcttctct	gggaagacag	74220
aagaaaagtc	cccagggaag	aatactacag	acttggcctt	agggacagct	aggggtgcag	74280
attgctgcca	actgcatttt	ttctgaagtt	ggccatatgg	ttgcagtga	tggatttata	74340
gacagagtat	ttctgtgcat	ataagagcaa	ttacagttgt	aagttgatat	ggataagtga	74400
aagttaagca	cttctttcta	aaaagagaat	gcaattcatt	ttccccaat	catttcaatt	74460
agtctgantg	ggcatttgaa	cttgttgtct	ttaaaaagtg	aaatctttac	ctctgatctg	74520
gtaagtatcc	aggcaatttc	ttgtgtgcca	cccaggaggt	atctggggag	tgggcatttt	74580
ctgactgagg	cattggctgc	catagcatca	gagcagcctt	ccaggcagtg	gcctggcaag	74640
gggacagagg	ctgggtgggag	cagctggctg	agtgcagcca	gtaatggcat	gtgcatggct	74700
tgtagagaat	gtagaagcaa	taatgaagcc	gataaaaagct	ggtctgcatt	ttattattat	74760
catgcgcggg	tggttctaaa	caatgtcagt	gataaaattac	tcttccccat	catggacca	74820
tggctgccac	tgctccaggg	aagtgccttt	tattccgttt	ggtgttttagg	gagggatgga	74880
gttggctggc	ctttgtctgaa	aggcctacca	gtttgttttc	tatttggcaa	aagaagaaat	74940
gataaagtty	tagagtttaa	accagactca	gatttgagtt	tttttttttt	tttttttttt	75000
tttttttaag	gctacagaac	tgtgctttcc	ttgggcagta	aaagaggcaa	tgggcaatgt	75060
gggacctgat	ngacaaanagg	gaannngnnn	nennannnn	nnannngctgt	cttaggggtg	75120
gcatggagga	ggtgctgctt	cacagcagag	agaggtatgg	ctgtgcttgg	agtgtccact	75180
tagacaactc	ctgjtctgtgc	agccaggcca	tcgagatgct	gtttccctga	cctgcaggct	75240
ctggtcttgc	acatggatgt	ttcttctggg	gcaggagaca	gaaaggtagc	aacaacccct	75300
gatcaaagcc	tcagtccttc	cttattttact	ggagagcccc	tgctgattga	ccagaggcac	75360

agctggggat	atttccttta	cctctgtagc	aagagacagc	gtgggtgcaga	ggaaagtgc	75420
agcatacatt	accctgtggc	tgcattgactt	tgtgaatagg	ttagtttagca	cccttttcagc	75480
cacttcttct	tacctgttaa	tgagataaaa	catgtaatgt	cttaaaaaaca	gtattttggca	75540
cataggaagc	acttagtgaa	tatgaattat	gatttttttt	ggagtgggtga	catctcaacc	75600
aagccattta	acccctcagc	cttnactttc	ctcaactata	aaatagcagc	taacttgaaa	75660
tgtaaaactat	aaaacctaat	gtagtatctg	gcacatagta	gattcccaat	aaatgagagc	75720
cagtattctt	tctaagacag	tgatgcattt	ctgagcacct	ggccttggtc	ttctgccttg	75780
caatttatgc	agcagttgaa	atagactggc	tgatgggggt	aagttgtcaa	gcagactttc	75840
tgatcttagt	ggaggagact	gccttaaaac	aacactaatt	tcctttttct	ttctttttct	75900
tttcttttaa	gacagagcct	cgctctgtca	ccaggctgga	gtgcagtggc	gcagtcttgg	75960
ctcactgcag	cctctgcctc	ctgggttcaa	gcgattctcc	tgccctcagcc	tcctgagtag	76020
ctgggactat	aggcatgctc	caccatgccc	aactaatttt	tgtattttta	gtagagatga	76080
gatttcacca	tggtggccag	gatgggtctcg	atctcctaac	ctcgtgatct	gcccgcctag	76140
gccttccaaa	gtgctgggat	tacaggcatg	agccaccatg	cctggccttc	tttgagaagc	76200
tggaagacatg	agtttaagtgg	tgaagaagcc	aaatctgtat	ctaaaaaccc	tacagtagtg	76260
tgagagagctc	tgaggagaga	aggtccctta	gattttgagt	gtattattat	gtcagtgcct	76320
gtttttacatc	tctctgttca	cgagtatgt	ccccctttct	gccttgagc	tgtttcttaa	76380
attctttctt	tctttgcttg	tcttgagca	caaaacaggc	ttcagtatag	ggggaaatgc	76440
acagaaacac	tgcccttttc	tacaggaaat	cagtaacttt	ttactgattt	tgtttttatt	76500
tacttttttt	atttggttaa	atttattttt	agtttttttt	tttttttagag	acaggggtctc	76560
tttctgttac	ccaggctaga	gtgcagtggg	gcccttagag	ctcactgagc	tcactgcagc	76620
ctcgaattcc	tgggctcaag	tgatcctcct	gccttagcct	cccgaagggc	tgggatgaca	76680
ggcatgagcc	actgcacctg	gccaaacttt	tgctgattgc	gaatagcact	cttgtcaatt	76740
tcggagagaaa	gctgagactg	gcatagttca	gtatggatcc	ccacttagag	acctgtgttt	76800
atctgcactg	acaccccatc	acagcatgat	gagcttggcc	ctcctgtgct	gtctctccca	76860
gggctgggag	gatccttgaa	gctgatctgg	tttgaggctt	tgctcctcatt	cacctccttt	76920
accacacacc	caccttccca	gggcggggag	ctaccactca	ctaagtagcc	cattctgggt	76980
gttgacagct	ctaattgtta	gaaaatattc	accaccctgt	tatgctttct	agagaacaag	77040
tctaattctg	ttttccttga	aatagtcgaa	gacagctctc	atgtttttct	ttccctgttt	77100
tcccaaagtc	catgattttt	taggcaaaat	ggcctccttt	cctcttatgg	aatgtttttc	77160
ctccccattt	ctgcctctcc	tctggttggt	tttcagtatg	tctgtgtgct	tcttgaagtt	77220
tactggaaat	tatgaaagta	ttctggcaca	ggagggaag	ggattttttg	ctcccttggt	77280
ctgagtgtca	catttcggtt	aatgcagtct	gagattgtat	taggcatttt	ggcatttcacg	77340
tcacgtgtgt	gactcatatt	ccatgtgcac	tcaaacaaaa	ttgtgattat	tttaaatagg	77400
cagaattgca	agttacgtgt	tctccatttc	tttggtgtat	tggtggcttt	ttgaactaaa	77460
gggaaaaaatg	tcttttttct	gttttacatg	tttagattcc	ctatgctatc	ctatcctccc	77520
aaaaccattt	tagattctga	ttttgccatg	tattatatct	gatactcctt	tctcgtcac	77580
tagagatgtg	ataaacaact	ctctttggcc	tcattccagt	catcgataac	tgtgggacaa	77640
agacttgaa	cttggatcag	tccagtggag	actaaccacc	cctgtagacc	cttttttctc	77700
caactataaaa	atagcagcta	acttgaaatg	taaactataa	aacctaattg	agtatctggc	77760
acatagtaga	ttcccaataa	atgagagcca	gtattcttct	aagacagtga	tgcatctctg	77820
agcacctggc	cttgttcttc	tgcccttgca	tttatgcagc	agttgaaata	gactggctga	77880
tgggggtaag	ttgtcaagca	gactttctga	tcttagtgga	ggagactgcc	ttaaaacacc	77940
actaatttcc	tttttctttt	cttttcttct	tttttttttt	ttaagacaga	gcctcgctct	78000
gtcnaccagg	ctggagtgc	gtggcgcaat	cttggctcac	tgacgcctct	gcctcctggg	78060
ttcaagtgat	tcttgattct	gtagacacta	ccactcaggc	ctatattgta	atcagtgcctg	78120
ggccactggg	ctcctgcttc	tgtgatccag	ttgggaagtt	tatcttggtc	ttcccttcag	78180
cttgcatctg	ctaaattcgc	tggactatac	acaggtgatt	tgtagatatg	gggatctcta	78240
ctcaataact	ctcatgattt	ccttggctag	agcatcattt	tatttccact	tattggaaga	78300
gaccttagag	accagttagt	tcatttatag	ataaattagt	tgattctgtc	attcaacctt	78360
tatatattga	gcgtctccta	tatgcgaatc	actgttctaa	gtgcccagac	acagaggtgt	78420
ccaaaacaaa	tatggccctt	ctccatatgg	aatttctatt	ctagagaaga	atctgaccca	78480
gaagggggaa	gtgactgtcc	caagtctaca	caaccacaga	agggatatct	tgggaataaa	78540
tcacggctaa	acccccctgc	tgctccaggc	agttctcctt	ctacagtgc	ctattgtgct	78600

gttttaataa	tctttcaact	gggaagaact	cccatttcag	gaattaagcc	gtggacaaat	78660
cttttaatta	tccttgaaat	catcctaata	agaaatccaa	ggaggaagtc	ttacaggggtg	78720
cctcaccac	ttttctcatc	actggaactt	tttagacatt	ttattatttt	cttcctaaac	78780
cagagtacag	gcacacaagt	tgagtgggtg	ggtggctaaa	ttaattaatg	tttgcaaggc	78840
agtgtgagaa	gcattcattc	atcttaaata	cctatggtga	ctgcaactca	gatgtaaaaa	78900
ttggataaat	cctcagaaac	cctagggaaa	gtgacatgtc	tgtattttgt	ctctgtgaga	78960
tacagactgg	cagagataag	tgtttctctg	ggtgagtttt	gtgtgggtatc	tgggatgatt	79020
ttaggcagta	cgtggatgag	aacttttaat	tttaaccac	atccaattgc	aatttcatgg	79080
aaattattgc	ttaggaggat	gttcaacagg	aaaaatataa	ttaaagttaa	ttcaaaaagaa	79140
acattttctg	tgaatatggt	aaaacttgtg	agagtagttt	gtaaatgatt	gaagattgga	79200
aaacattggt	ataagagtga	gtgtggggtt	ttgtattaag	attcattttg	ggaagaaatc	79260
catgctgcat	ccctcatgaa	gtgtgaactt	tgggcatgtg	ttgattcttt	ctggcccaga	79320
gtttacctga	agatttagctg	ccctgagggt	cactgagcat	taaattagat	gatgtctgtg	79380
gatgactgat	agtgaagctc	atagcccaca	gttgacacat	aataaattcg	agttgctttg	79440
cttccccctc	tgttccctggc	tgactgtttg	gcctttgcc	cttggtcggc	ctctctgggc	79500
cttaagtttc	tttgccctga	aattggaact	ttctttggtg	aaacaaccag	aaaatgcttc	79560
agcccagaaa	cttggtcagt	acttggatgg	gggatcacct	gggactaccc	aaggatgtgg	79620
gctgtctgct	agactatagc	cccttgaggg	caaggtgggc	gccttgctca	tggttccatc	79680
ctaagcccca	gcacagtagt	gggtgcatgg	tgagccatta	gtgaatcttt	gtggaatgaa	79740
ggtgggagaa	aataaaatac	ctgtacttca	caggggtattg	tgaggggtcaa	gtaaaagtgc	79800
tttaaaaaat	tgtattatat	agtttattcc	cttggtgttag	cccaggtcaa	cagagcctac	79860
gaataataat	gatgacagaa	gttcttcaaa	aagtcttgcc	cttctttctt	tcacaaaatt	79920
gccccccaga	gctttctgga	agggcagcca	tgaaccagaa	ggcctaaagt	agattttactg	79980
ggaagctaaa	aatattttact	ttatttttca	tagctccttt	caaggtcctc	tctgggggtc	80040
ttagcaatat	gtttacacag	tggtatgttt	ttgtaagggt	tgcaaaagta	agatttttta	80100
aaaatactat	cttggttttaa	aaagagagcc	ccctaccaac	ttgtgtcagc	ctcaggcccc	80160
cacctgcatc	tgctcctgcc	agggcatggt	ggggcaagaa	gcactgctcc	ccttccaaag	80220
cttctctcct	tgccttgag	tcactctcac	tccccactcc	aagccacctg	ccatcgctgt	80280
gccccctctc	tggtgaatct	ggcattctta	ggtgggctga	gaagcagact	ggcccaagct	80340
aaggcccttc	tgatggggtt	gttgctgctg	agaatcatga	ctgggtggga	gaaggagggtg	80400
accctttngc	tgtcttattt	ttactgtgta	tttcttttct	agctacttaa	aatgtattgc	80460
ttagtgtata	ctaattgggtt	cattagcctg	cttctactg	aacatttccg	ctcaggcatc	80520
cactgtgtcc	caaggcctgc	tcctctccca	tattctgaaa	tctggactac	agactctcat	80580
tcaactccag	gttgactgtt	ggacacagtc	ccctcttgag	caggtacctc	cttgacgtgg	80640
ttgggacgtc	ctacttggtc	catagtggg	aagtgcata	gctggagctg	aagcctcttg	80700
ccttcccggg	atagggcgct	ctcacatccc	ctctgagaag	ttccccagct	tcctctctgt	80760
ccccgtttcc	acacttagcg	aggctcttgt	ccactgctac	atccccata	gccagtcctt	80820
cagccttgcc	attgcttatg	ctggctgga	aacaattcct	agacttgtgg	ggcatctggg	80880
gaagtctctc	atcttttttt	agctggcatg	acccaagtgg	tgtgggcagg	gctgtggatt	80940
ctatgggtgtg	gctggaagcc	aggtagcctc	tctctactgt	acatggaact	cagcaacttc	81000
tgagtcaagc	aagatcttag	ctctgcaggt	gtcttgccct	gtccaaagtt	atggccacac	81060
cagtaccttt	taactctaga	agcccagtaa	gtgttttgtg	ggaccgcaaa	gatcattttc	81120
tagacctgct	gaatatgcct	agaacgggta	gggatggctt	tcacgctgtt	cctagggctg	81180
acaagtcaca	cgtttctggg	ggtacatata	caccgcggtc	cctgtgaatg	gcactctcca	81240
tgagaactgt	gatgatttga	gttgaatagt	gcacagccta	catggttctc	tgccatggcc	81300
tggagtctct	tatcttgctt	tctccagtga	ggactagggc	tgcaactggc	ctactttggc	81360
tcctgacttg	gggattctctg	aaataccttt	tttttttaag	gttgtggagc	tctctgaagc	81420
ttataaggat	tttgccagga	aaagataaga	aatatctttg	ggcattttgt	cactgtgctg	81480
gagatgaacc	ctttggagga	catatcacct	tgttgaggtc	aaggggcgga	aaggggacagg	81540
actggcagag	agatccgggg	cagcagcctg	ccatcccagc	tgagtatgga	gtttctctct	81600
cccttcagct	gcacttttgt	gtggagtcat	tggtctagct	gccacttccc	ttatgttcat	81660
ggcatgaatc	tggcttggtt	ggcctttctt	tttttttttt	ttttttgaga	tggagtctca	81720
ctctgttgcc	caggatggag	tgcattggag	gtagtgtgtg	gatctcggtc	cactgcgacc	81780
accgcctcct	ggattcaagc	gattctcctg	cctcagcctc	ctgagaagct	gggattacag	81840

gcgcacgcca	caacacccctg	ctaattttttt	aattttttatt	tattttatttt	ttttcaagggc	81900
agaagaattt	ttcttagtac	agaacaaaat	ggaatctcct	atgtctactt	ctttctacac	81960
agacacagca	acaatctgat	ttctctatct	tttccccaca	tttccccctt	ttctattcga	82020
caaaactgcc	attgtcatca	tggcccatcc	tcaatgagct	gctgggtaca	cctcccagat	82080
ggggcgggcg	ccgggtagag	gggtcctcca	cttcccagaa	ggggcgggcg	ggcagagggc	82140
ccccccacct	cccggacggg	gcggctggcc	ggggcggggc	tggccccccac	ctcccccccg	82200
gacgggggtg	ctggccgggc	gggggctggc	ccccacctcc	ctccccggac	gggcgggctg	82260
ctggccctgt	aatnttttgt	attttcagta	gagatggggg	tttaccatgt	tggtcaggct	82320
ggtctcgaac	tcnncnntng	acctgttgat	ccacntggn	cctcangcnn	ctcccaaagt	82380
gttgagatnt	acaggcatga	gccactgcgc	ccggctctgt	tnnttttgtt	tgtttgtttg	82440
tttttgtttt	tgttttgaga	cggagtctta	ctctgttgcc	caggctggag	tgagtgagac	82500
ggcacgatct	tggttcactg	caacctctgc	ctcccgnggt	tcnaaaacaat	tcttcctgcn	82560
ctncagcctc	ccgaatagct	gggattacan	ggcacttacc	accnaggcct	ggctaatttt	82620
tgtatttttt	agtagnnang	acgggggttt	gcnatgttg	gccatttgaa	ctcctgacca	82680
tctttngaac	tcctgacccat	gtttgcncat	gttgaaactct	tgacttcagn	gtgcgttggc	82740
cntcccaaag	tgctgggatt	acaggtgtga	gccaccatgc	ccagcctggt	tggcctttct	82800
gatatgngnc	ntcntgacta	atcttttttg	aaattnagnn	ntccccaggg	ttatactgga	82860
ttttacttag	ggaaaagggt	catgcncctct	ctggctgtca	gnatttactg	atagtactaa	82920
ggnactcagn	tggggtgnnn	gnacctttga	ttcnmtnggt	ttgatttttg	aaaatncaaa	82980
aagacgtgag	ctccagggag	cagggtggct	ttgggtganca	tggcaagata	gttggtgtgt	83040
gcnagggagt	tgagggaggt	gggtagaaaa	ttaacatctt	gtanaaatatt	nnncnctggg	83100
aaatatacct	tcgtgttaag	agaacagact	tggcagncn	nannngnnan	nnnnngggc	83160
taggttcaaa	tcttggtctg	atgcttatca	gctgtgtaac	cttgataat	tcatacatc	83220
tctgtgcctc	agtttcctca	aatggaataa	caatagtacc	tcctcagga	ctattgtggc	83280
aaattaatgg	acgaataagg	ggaagcactt	agtacagtgc	ctggcccagc	ataggtacca	83340
ggcttggtct	taagctcact	gcatttttac	aatcatcata	aaatgcaggg	gatacacaca	83400
tgaaggagcc	gaagttcaga	gaggccaagt	aacttgccct	agaaagcaca	gctggcaagg	83460
ggcagtaata	ggaccagaat	tccagttctc	cgtgctctgt	tgttggtata	tcctaaagag	83520
agcagctctg	agtagccaga	agcttcccta	aagtcacagg	acatggggca	tgggctggct	83580
gggatgagaa	aggagacaag	agggtctctg	aaagaaatgc	cagattcact	ccacttctct	83640
gcttcaggca	ccgatgggaat	gtttcccaag	gcccattctag	aaagaacatc	ctgtgactca	83700
cagccaactc	tcattttctg	tctgaacccc	ctcaccatt	caggcagctg	ctaaagtga	83760
ggttacagcc	tcagactata	ttttctgtcc	ttgtggaaac	ccagtgtgtc	atcttggttg	83820
gagatctggt	gatacatgtg	tcaacattat	gtcatcaaaa	tggaaattct	ttgaaatctt	83880
taggtgattg	caattcacgt	tctgtatgta	tgcacttgtc	aaaagttttg	atttgaggcc	83940
ttagaatttt	atatttgga	acctttccac	taccatgagt	tttcccagac	ctgtcaaagc	84000
caggctgcat	ctcagaaacc	aggtctttga	tttccatcca	gggcaagggc	ctgggccag	84060
ctgggctgta	agcagggtgg	gggtggggagc	aacgctgcac	tgcaatgttg	aaatattact	84120
tgaactaaat	caaatcaaag	atcagcttta	ctcagacaag	aatagaaaac	acaattgcat	84180
tcgattacag	aatagtgtgt	atccccacaa	atatcagact	gcctttaaaa	agttttgaat	84240
tgttaacatc	aagaacagtg	ttgcgtgtct	cctgcttttc	cagcataagg	tttattttat	84300
ctgtgggtgg	caaagagcaa	tttgggagtc	cagtttggtt	ctcattgaaa	gctttcccat	84360
ttctggctct	cttgctcactg	ttgcattgag	gcaccaaag	gcaatctcag	tgcgacacta	84420
ttcaacagac	taagttgcac	cggataatga	taccatttta	catttttcat	atattattac	84480
attgaaggct	tcaaacagca	ctagcagggg	caaattggta	ttattatctc	catttctattg	84540
atgaggaaac	cgaggctcga	aagggtaatg	tctgttgctc	aagattaaaag	agtaaagttg	84600
tacgttgaat	cggggtctga	ctcctaggct	tagcattttc	tccccacact	atgctgccat	84660
gttgcttatt	ccaacattag	gaagcatagg	tggcatcccc	agcttttgag	gccaatatca	84720
cgatgaagca	tttttaaaac	atctcattaa	attgctgata	tagtggaag	aaccaaagct	84780
ttgcagtcaa	agctgttttg	gttcaaattt	accacttggt	tgttctatga	ccctgagcaa	84840
gatattctcc	agatctgttt	cctcatttga	aaaatgggaa	taataatacg	tttctttata	84900
ggctgttctt	aaagattctg	gaaaataatg	ctaatagtgt	gcctaagtgt	tggtaaatat	84960
gagtcacttt	tctgtgcccc	caaagcacta	ctatgtccct	taataaattt	tgtaattttt	85020
aaaagttaga	aaaaaattaa	actattttata	cattgtgtat	gttaattctt	ccctagacca	85080

gccttaggaa	gaatctcatc	cccaacttgt	aaactcatct	ttttccgttc	tttttgtgcc	85140
tggacttctc	agggccctgc	aggctgattc	tagtcccatg	ttgtgtggtg	tttgaagtgt	85200
ctgggtccctt	ttttcagtga	gagaccagct	catccttggg	aactgaatgc	ctcaaactct	85260
cttttctttt	tctctcttcc	ccttctgttt	gatgtagtct	ttcctgtttc	tggactctgt	85320
ttcttcatac	ttcctatctc	ttaccttctt	ttcactcctt	ttgtcttcca	gctgtcctct	85380
ctcatttttc	tgcctctctg	gtcttcaggt	agagttttca	tctcagctat	cttcttgcct	85440
tttctgatgt	tgggtctttg	tttcttcttc	tcattctgtt	caggtccaaa	attcatttgg	85500
gtcaatgtta	tgtcttagtg	ttatcttcca	tttcttctg	agcttcaaag	ccaggctgac	85560
tgtgcccttc	cacgccctgg	ccagtgtgac	caggacatcc	tttccctctg	gggctgcact	85620
ggctcttttg	gggaattggt	accattcagg	gtcttcaacc	ctcattctag	ggacttccag	85680
taacttctcc	cacottccct	cttctcagta	agacatgggt	attgtcttat	tctgtttctg	85740
ctgctagaag	aaaattctcg	agactgagta	atttatacac	aatagaaatt	tacttctcac	85800
agttctggag	gctgggaaat	ccaaaatcaa	ggtgttgcca	ggtttgggtg	ctgggtgaggg	85860
ctgctctctg	cttctaagat	ggtgccttgt	tgtgcacatc	ttaggagggg	acaaacgcca	85920
tttcttcaac	tggcagaagg	gactgaagcc	tctccctcaa	gcccttttat	aggggtcctc	85980
attgtcaggc	ctctaagccc	aagccaagcc	atcgcacccc	ctgtgacttg	cacatatacg	86040
cccagatggc	ctgaagtaac	tgaagaatca	caaaagaagt	gaaaaggccc	tgcctcgcct	86100
taactgatga	cgttccacca	ttgtgatttg	ttcctgcccc	accttaactg	agtgattaac	86160
cctgtgaatt	tcttctctct	ggctcagaag	ctccccact	gagcaccttg	tgacccccctg	86220
ccccgtccca	ccagagaaca	accccccttg	actgtaattt	tccattacct	ttccaaatcc	86280
tataaaacgg	ccccacccct	atctcccttt	gctgactctc	ttttcggact	cagcccacct	86340
gcagccaggt	gaaaaaaaca	gctttattgc	tcacacaaaag	cctgtttggt	ggtctcttca	86400
cacagacgca	catgaaactc	atgggtatctg	tgagggggccc	taatgctatt	ggtgagggca	86460
ctgctcacat	aacttaatca	ccctttaaag	gccttgccctc	ttaatactgt	cacattgggtg	86520
atgaagtttc	aatgtatgaa	ctttgagggg	ggacacgttc	aaatcatagc	aggtgtgcta	86580
ttgccttact	agcaaagtaa	tctgggggaa	gatgagtaat	gtctcgttcc	acctctgatt	86640
ccagtgtctga	ctgattcttg	agtggcagag	aggggttgag	gtccaccgct	ctgctcacc	86700
gacctcttg	ccatctctct	ttagaatgca	agggcaggga	ttttgttaca	cagcgccctct	86760
tttgttatag	gctagctcct	gccttcaagg	agcactgaga	aaaatattat	ccctttgaac	86820
cacaacacta	gtattttggg	tactgtagcc	attcagaagt	ttgttgaact	aatacaagtt	86880
tatattat	gtaaaatact	agaaggaatg	tgtggttcct	aaagttatgg	tattcccatt	86940
ggttgaaaga	gaagancctc	ggcttcctaa	tgccttgga	ggttcaggga	gcataagcct	87000
aaatatcctg	gtttctcttg	ggaattcttc	acagcttgct	atctatgact	ttatcccat	87060
ttattttgaa	catgtttaat	tttcagcttg	tattttctca	aggagtatgt	gtgagtcagc	87120
attcagagta	cttaacacac	ttagtgtcat	tagtgataac	ttaaccacaca	cgtataggaa	87180
gctagacctc	catttacaga	aaaatggagg	ctcagagagc	ctaactgact	ttcccaaggc	87240
cacataactg	gaaaattctg	gaactgagtt	tttccaggta	tgtcttggtg	tccctcggtg	87300
agccttctct	gtagagaagg	aagtgtctcc	tgggttgga	agcccaggcc	gggatgaaca	87360
gcatgggtgt	ccttaggctg	tgtgtaccac	acacccctgg	cctactctcc	cctgctctaa	87420
ggagtcacct	gaaggagcag	ctgcatcacc	ccgcctcacc	ccttctctct	agcaccaca	87480
aaccaggtct	tcccagagag	tgctcagcta	ttggtgaagc	aggcatcgct	tattcttcaa	87540
gaagacagca	gagcatcagg	aaaacaaaac	acaaaaaaa	taccataaag	acactggagt	87600
gtatttggtta	ccagcccttg	tataacagag	aagtatttca	aggtcttatt	tgtaaggctg	87660
gacaagctca	ggctgattaa	aaccacgagt	tagaatttgt	ctcccgtctc	caggccctgc	87720
tcagttgaca	gctcctagca	ggctggggag	ccccaccca	ccccacccc	aggggtccat	87780
tgaagaagac	catctggggc	tgggatgctg	atgtgatttt	ccctacttct	cctttttttt	87840
catttgccctc	ctccacccac	ttctaaagca	gctgattgct	ctgggtcctt	ttcatgttga	87900
gcaaaagaga	agacagatct	tgaacactga	gctggggact	ggagggcact	gaccgagagt	87960
aaccccgctct	ggctcagctc	agctcagcaa	agggctttcc	tcctccgcct	tcctgagctg	88020
ctctccctcc	tctcctttcc	tccttcttcc	ccagcctccc	ccaagctcct	tcacccctct	88080
cttccctctc	ctccctctct	ccaccttctc	tgtcctctat	gctcagagaa	ctgaaggaa	88140
actgaatggc	ctggaaagca	ggacctcgcc	cccacccgc	gtcatacccc	tcctcctgca	88200
cgtgcaaatg	tgttctctcag	cttgggtccca	gaggcctgga	cctgggtccc	agaggtccca	88260
gctgggtccc	cggcttggtc	ccagaggcct	ggatgtgtgg	caagaagctg	aggggtctgc	88320

WO 01/15676

PCT/IB00/01492

ttttttttga	gacagagtct	cgctctgtca	cccaggtctg	agtgcattgg	tgccatctct	91620
gctcagtgca	accactgcct	cccacgttca	agtgatccct	ctgcttcagc	ctcccaagta	91680
gctgggatta	caggcaccca	ccaccacact	cagctaattt	tgatatgttt	agtagagact	91740
gggtttcacc	aggctgatct	caaactcctg	acctcaagt	atctgcccac	ctcaccacgc	91800
caggttttat	taaattctga	tgcttgggtc	ttaccctagc	agttctcatt	agttgctcca	91860
tggtgtggcc	tggtgtttgg	gattttttgt	aagccccag	ctgagtctaa	cgggcagtc	91920
tggttgagaa	ccagtatact	acaccatgtt	gccttcctgt	tttcacacag	gttggtgcta	91980
gtgtgtgagt	ctaagcctac	atgggtggat	atccacgtga	tcaggctgca	agttctttgt	92040
agtggaggat	ctttggccct	ccctgctgct	tcccaaccca	gcgaacctac	cacaccatgc	92100
acgtgcacag	ccaagggttg	ttgactgttt	aatcagttct	tggtttctta	tgtctcatcc	92160
gggggattca	ctgataggag	gctggagctt	gatcacatcc	agatgttctc	atcttcagag	92220
cctgttaaca	taacagaagt	cttataaaca	tgctgagcac	actcactggg	ctggagagtg	92280
ttgcaggatg	acctaggccc	attgcagggg	tggtcctggg	cgccctccca	cactttctgc	92340
accctgcttg	ggaaggaggg	agctgttttg	aagttccctg	gtgcaatatg	atgtattgct	92400
ctggctctgc	tcaggaggaa	gctatggccc	acctagtcag	tgagggttag	ctaatacgtg	92460
tattctgttt	ctgttgaggt	ttcacagagg	ccttttttga	cccttcattt	tatagataag	92520
gcagtggagg	cacaactaca	tgaaatgact	cgacaaataa	atggatttag	aacccaggtt	92580
tctgactccc	agggtgggtg	tttttccatg	gttgtacagt	gattaatgtc	taccttttca	92640
caccagtcct	caactgaaga	caccagctta	caccttcctt	cctgtttctc	ccaagaacag	92700
aaagtgacct	cggatgtcgc	tttctgttcc	tggaaggcca	gttccagtgg	ttagaagtc	92760
tggttactcc	tggtgtgtgg	cctggggatg	gtcctgacat	ccctgggctc	ttcctggacc	92820
tggtccagcta	aaaggaaatc	tcctatgatg	gtactcagat	acttttggaa	ccttgtcagc	92880
cctaataccca	tctcctagt	tttagtattc	agctaccctt	cactgggcag	taattctgtg	92940
ccaggcctga	tctgggcatt	ggtgtacta	agaacgcata	ttccctatcc	tataggcata	93000
gtctggtaga	gacaacatgc	aagtaaaaca	atgttccctt	aactgtgggt	ccacacctcc	93060
ctcccccaac	attaaaagt	taagggatgc	ttattcaaat	gtagatttgt	aggctctgca	93120
ctctagacct	actatttcag	aatctctggg	gactgggccc	aagaaactgc	attttcgc	93180
gctccctaaa	tgaagcttag	gtgctctgag	gtttgacaac	tgcaagtag	agcctaagc	93240
taacagtgta	gagtcacatg	tgatgggaag	catcaggtag	gtagcagttt	gcaggagcac	93300
tgattctgag	ggacactaac	tggtccctaa	aacagctact	ggctgtcatg	aggaataact	93360
aggagctagc	catagagggg	tagcagtgaa	tcatttctct	agcgatgtaa	atcttgctca	93420
atttattctg	tctatataac	tcaatattac	tgaagtttgc	ctaaagcaga	atacacctgg	93480
atcatcacgc	atttatgaga	gactggctgg	gctgtcaggc	cctcctgtta	ctttatctct	93540
gcatgtgacc	ctcttasstc	cgcggtataa	ctcctgtcct	cattaagcct	cacactgtag	93600
ccccattttc	agatcaaacc	tggttctctt	ctggtaaaatg	atttcagttt	gcaaagtttg	93660
ccctctagag	gttgcttagt	gcctggccat	gtgggtcag	ttcatgtggt	cctgatgagc	93720
tggtttttat	tttattacaa	agaagttagg	ctgttaggag	agtgggttgg	aaggagaaga	93780
ggtagacagc	caaatgagat	gagtcaggga	aaactatact	gtttcggagt	catagggctc	93840
ctaccaagca	tctggtcaga	aacctctcat	tttgagatc	aagaaattga	ggttcagaaa	93900
gatgacatga	ggtacgcagg	gacgccacca	gacacagcct	ccaactctag	aaactaaaat	93960
tctggattct	tagtgctgct	ttttctgttt	tggtgcactg	gattgaagcc	ttttctaaact	94020
gtactcagag	ggcctattat	ttaggagat	tccgtatgaa	atccttttagc	aatcaaatca	94080
tttaatatggg	ctgatgggtt	aaatatatgt	taatgtgttt	tcctaaagcc	tggtcagacct	94140
gggtttttgga	gctttgtatc	acatgtttta	tggttggaa	gaaaatgaga	ccatgtctgt	94200
gaaggcactt	tgatatgcgt	aatgcactct	gccagtgttt	gtcaaaacat	gggtcccagg	94260
tcagcagcat	cagcatcacc	tgtaagtgt	tctccagtcg	catcccggcc	caggmsmggg	94320
ccmrcteny	aggcytgtg	smggcsmgg	nsggnntg	nccggcccg	cccggcccg	94380
cccgcccg	cagtctgcat	tttaacaagc	tctccagtg	attctgatgc	atacttaagt	94440
ttgagaacca	ttgcttgttt	tgcatataac	aggagattag	tctctgcagc	ttgtgggaat	94500
aaagctttta	atctctccaa	ttttagctct	gtgaaaaggc	agtggggaga	caggaatgaa	94560
cggactagt	ccacaaagct	caggtggggt	gggtgagatc	atttagaaga	gaaagaccgg	94620
gcatggtggc	tcacgcctgt	actgtcagca	ctttgggagg	ccaaggcagg	ttggatcaca	94680
aggtcaggag	tttgagacca	gcctgcctat	catggtgaaa	ccctgtctgt	actaaagata	94740
aaaaaaaaa	aatttgccag	tcatggtgat	gcatacctgt	aatcccagct	actcgggagg	94800

ctgaggcagg	agaatctctt	gaacccggga	ggcgggggtt	gcagtgagct	gagattccac	94860
cattgcactc	caacctaggt	gacagggtga	gactccgtct	caaaataaaa	aaaaaaaaag	94920
aaaagggaaag	gctgtgtgtg	tgtgtatgtg	tgtgtgtgtg	tgtgtgtgtg	tgtgtaacag	94980
caccatcaca	ctgtttgagt	tgaggagcac	atgctgagtg	tggtccaaca	tgttaccaga	95040
aagcaatatt	ttcatgcctc	tcttgatatt	gcgatgctcc	cctatctcat	tctgtgtgtg	95100
gttttagccag	gcaactgttg	atcatcaata	ttatgataac	gtttctccac	tgccccattg	95160
tgcccacttt	tttttttttt	ttgagttact	tactaaataa	aaataaaaaca	ctattttctca	95220
atagacttga	agcttcaaga	tttcctgggt	gacaatgaaa	ccttctctgg	gttcctgtat	95280
cacaacctct	ctctcccaaa	gtctactgtg	gacaagatgc	tgagggtgga	tgctattctc	95340
cacaaggtaa	gctgatgcct	ccagcttctc	cagtagggct	gatggcaatt	acgttgtgca	95400
gctactggaa	agaaatgaat	aaaccttgtt	ccttgtaatt	gtgggtgaagg	ggaggggagg	95460
agtttgaata	caacttcact	taattttact	tccctattca	ggcaggaatt	gccaaccat	95520
ccaggagtgg	aatatgcaac	ctggcgtcat	gggccagctg	gttaaaataa	aattgatttc	95580
tggtttatca	cttggcattt	gtgatgattt	cctcctacaa	gggatacatt	ttaagttgag	95640
ttaaacttaa	aaaatattca	cagttctgag	gcaataaccg	tggttaaggg	ttattgatct	95700
ggaggagctc	tgtctaaaaa	attgaggaca	ggagacttta	gacaaggggtg	tatttggaga	95760
cttttaagaa	ttttataaaa	taagggtctg	acgcagtggc	actgagttga	gaactgtttg	95820
ttgttttgca	ttaaatagga	gatcagtcct	tgcaagcttg	gggaataagg	ctttaaattc	95880
ctccaatttt	agctctgtga	gatggcactg	gggaaacaga	aatgaacgga	ctagtgtcac	95940
aaagctcagg	tggtgatggac	gagatcactt	caaaggctctg	taatcccacg	tctataatcc	96000
cagcactttg	ggaggccaag	gcgggaaaaa	cacttgaggt	caggagtctg	agaccatctc	96060
ggccaacatg	gcaaagcctg	tctctactaa	aacttatgaa	attagctcag	cgtgggtgcc	96120
tgctcctgta	gtcccagcta	ctcgtgaggc	tgagacagga	gaatcggttg	aacctgggag	96180
gcggagggtt	cagttagcca	atatcacgcc	attgcactcc	agcctggctg	acagagttag	96240
actccatctc	aaaaaaaaaa	aaaaaaaaaag	aattttataa	aatcaggaaa	taatattagt	96300
gtttatgttg	aatttttaact	ttagaatcat	agaaaacttc	ctctggcatc	attattagac	96360
agctcctgtg	cagtgggtag	caccagacct	agcttgcatg	gttattgatt	tttcagagac	96420
actttttgag	cttattctct	ggcagaaagg	ggaactgctt	cctcccttat	ctcgtgtctg	96480
catactagct	tgtctttaca	agaagcagaa	gtagtggaaa	tgttttattt	tgaaaataag	96540
ctttttgtct	catatgatct	agaattttta	aaattagaaa	aatgtgctta	ctgcgtgccc	96600
ttctgaaact	aggaaaaatat	gccttgtgtt	taccaattgt	gtggttagga	gatgggccaa	96660
aggcatcagg	cttttgaaag	tagttgcatt	tacataaatt	tccattgccc	cctggcaatt	96720
tcatactctg	cacatctaatt	cagtttaaaa	taaggggcat	cctaagcatg	gagatggccc	96780
ttggatgggc	cttggagttt	ctgtattttc	agtattcttt	tttttgagca	tacaagacat	96840
ttattgaaaa	attcttggga	tcaatacttg	tgtaaaggaa	ggaaagggaa	caaagcatga	96900
ttgggcagag	gcagaagatg	acatcaacaa	aggccctccg	ttgtcagtat	tctttttttt	96960
tttttttttt	tgagttggag	tctcgtctct	tcaccagggc	tgaggtgcag	tggtgtgatt	97020
tcagctcact	acaacctctg	cctcccaggt	tcaagtgtat	ctctgcttca	gcctcctgag	97080
tagctgggat	tacaggcatg	caccaccaca	cctgggtaatt	tggtgtattt	ttagttagaga	97140
cgggggtttca	ccatgttggg	tggtccagact	ggcttgaac	tcttgacctc	aggtgatccg	97200
tctgccttgg	cctcccaaag	tggttgaatt	acagacatga	cccactgcac	cgggctgtt	97260
gtcagtatct	ttaaacatag	acactaactg	taggctgaca	gcctagcagc	aaggaccagt	97320
taaagaaatg	agtagaactg	aagtgtgctt	gagtatctct	ggcagtcagc	aaaaacttaa	97380
tggggaatcat	ggtaggccaa	atgttctgca	gtattttcaa	agctgcatgg	gttttgagag	97440
gcttttggct	catcactcac	cttaggttgt	tctacaagca	catcagcctg	ccccaaattt	97500
aacagggcag	ttagtaattg	tgtaataaag	agtctgcatt	gttcattcct	tcaacaaata	97560
ctggctataa	tgtttcagca	ctgtggatgc	aaagttagca	ggataaacag	gctcttcttt	97620
caaagcttgt	ggtccactgg	accacgtatg	aagtagaata	gttttaggtcc	agaaaggcaa	97680
ttaagtaaaa	tatgaccaag	aagaggctct	ctagtgggtt	tggtataaag	aaaagataag	97740
aatgatttag	aattggccta	tcaatgagat	aagaggcctg	gctttctggc	actctgctct	97800
agggcaagta	aaatggagaa	ttccaaatc	tgaaattgtt	agaacatagt	tctgtgtctt	97860
agttaaatat	ctacacttac	agataaatag	cataaatgct	ttctcccat	atttcagccc	97920
agtccactct	aaagacaaca	taaattgcaa	aatagttagg	atgttgttca	tctaataaaa	97980
gtggttccag	gaattcagac	tctggattcc	tgtttgccaa	atcatgtgtc	ccactcttaa	98040

gaaaacgagt	tggactctgg	atTTTTcttt	gcaagagggga	caagagtgtg	ggagatactg	98100
agttaatgca	acttgcaggt	tttaagtgtc	ctgtcattgt	gccttgtgct	ttgatacatt	98160
ctgagtttca	gtaaagagac	ctgatgcatt	ggactgttgc	aatggaacct	gttttaagat	98220
cttcaaagct	gtattgatat	gaagttctcc	aaaagacttc	aaggaccag	cttccaatct	98280
tcataatcct	cttgtgcttg	tctctctttg	catgaaatgc	ttccaggtat	ttttgcaagg	98340
ctaccagtta	catttgacaa	gtctgtgcaa	tggatcaaaa	tcagaagaga	tgattcaact	98400
tgggtgaccaa	gaagtttctg	agctttgtgg	cctaccaagg	gagaaaactgg	ctgcagcaga	98460
gcgagtactt	cgttccaaca	tggacatcct	gaagccaatc	ctgggtgagta	gacttgctca	98520
ctggagaaac	ttcaagcact	aatgctttcg	gaatgtgagg	cttttccttg	gacagcatga	98580
ctttgttttg	tagaaaagta	cggctggctg	ggagtttgtg	atataattta	gttcagtggg	98640
attctaagtg	ttcttagtgt	tctttcagac	ttttgggcca	tctcccaaag	gggtgaatggg	98700
aagaataagc	tgggtgtggc	tgagtttaag	ccaaaagtgt	tttgtgcttg	tttcaatcag	98760
agaagacctg	ctttttcatg	tttttactat	tataatacta	agcaagagct	catttgaaaa	98820
cagagttctt	catattttaa	aaaaaaaagt	cttgaaaacca	ttgatgggaa	gatggatata	98880
tatttatgtt	taaaaaccca	tcataaagat	gacattgtgg	gctgtcacag	ttggaaggcc	98940
ctggaattag	atgagaccac	actattttag	ttacttagta	ataacattgc	aaagaaaaat	99000
tccgacgaag	ttttttcagc	ctaggaatca	atagttcaga	gaagcactct	atgagaatac	99060
ccatttcatt	ttaaccaaaa	aatactgggtg	agcctgagca	gtttgggtcat	cagagtgttt	99120
tatatagttc	cagaacaaat	atgtctctag	gtgttctgag	agctctgggtg	aaattcctct	99180
cgctacccca	aacatcatca	tttaatatcc	aggattcttg	ttttctactc	accagataga	99240
ttctcttaaa	accagggaaa	gattcctgga	ggaaggatgt	atctggaaag	agatgttcct	99300
tattataata	aaatgaaatt	gtaatactct	tggattttgt	gcagcacgaa	ttctttatag	99360
agagttgggtc	ctcccagaga	attaaagaata	ctcagtttct	ggaccctgtt	cccagatcat	99420
accctagaat	gtgaccttag	aaacacactt	caggattcat	acctttgatt	gaccatcaaa	99480
aagtttttgt	atcggtccagg	tgtggtggct	cacgcctgta	atcccaccac	tttcggatgc	99540
cacggcgggc	agatcacgtg	aggtcagcag	tttgagacca	gcctggccaa	catgggtgaa	99600
ccctgtctct	acaaaaatac	aaaaaatagc	cgggcgtgat	ggtgggcacc	tgtaattcca	99660
gctactcggg	aggctgaggg	aggaggtatc	cttgagccta	ggaggtggag	gctgcagtga	99720
gctgagatct	gtctcactct	gttgcccagg	ctggagtgc	gtggcgcgat	ctncgactca	99780
ctgcaacctc	cgtctctcat	gcttaagtga	ttctcatgcc	tcagcctccg	agtacctggg	99840
actacaggca	cctgbcacca	cgcccagcta	ttttttgtat	ttntagtag	acatagggtt	99900
tcactatggt	gcccagctgg	tctcgaactc	ctgagctcaa	gtgatctgcc	cacctcgggc	99960
ctcccaaggt	gttgggatta	aaggcatgag	tcaccgtgcc	tgggtcccatg	ttataatttt	100020
aaagtaaggt	atattttctct	acagggatct	ttgcaaccct	aagtaanctg	gcctaaaaag	100080
ttagagaagc	tgacttgtgc	agacatttgc	agcctgttgg	tcttttttgt	gctgtgaatc	100140
atagagggtg	aaaggttatt	atgaatggta	caaaactttg	ttacaaaacc	attttcttgg	100200
actgttttgg	gctgcttcac	tgcatgacaa	atgctcacc	tttcagctgg	aatgattgaa	100260
attttggaaa	agatgggtgt	ttttagaaga	cattgtaatt	tggtccgggtg	ctgtgcccac	100320
tcattccatt	tcacttctgt	ttactcatta	aacacctatt	gtgtacacaa	cccggtaaaa	100380
tccctccact	cacacaatgc	ctgaattata	ctcatagtag	aatgactgtt	tagccctcat	100440
catctgataa	ttacacagctc	aggtttcaac	ctgacagtat	ctctctggga	ggattagcag	100500
cgtgacagag	tgcagggaaa	tgcaccttca	gaaccgtcag	ctacactgtg	tcccatcctg	100560
ctgtgttgtg	gttgtgcctt	gtggatgcgt	tggtttatga	ccaggtattg	attaagggtg	100620
ctactaccag	gtgctttctg	catatctcgg	gtttgtggag	cactcaggtt	ctgcttctgc	100680
ccctctgctg	ttaccaagag	acctctcttc	aaaaatggggc	tcttgagtta	gagtagaatg	100740
agtgtaccag	attgttttgt	gtaaagatga	tttctgagga	aggctttagg	atgaaatgac	100800
ttccaaacat	tttgaaatgt	gactcttact	tattgaatta	agcagggcct	taattggaat	100860
gctgggactg	atacttgatt	tgcattaagc	agcctttttc	tattgctgct	tggnttgaaa	100920
tttcaacatt	tgtgatggta	gatggatgtg	acatgtgatg	acattgcaca	tgggcagtta	100980
actgtgccaa	gaagtgcagc	agtagcagca	accggagatg	caaagcccaa	catgatgggg	101040
agagaaactc	ttctttcaat	atgtgcttct	gtacccaaaag	tggaaatttca	cgagagacat	101100
attttgaaac	atttctcctt	ttgtgtgtgc	gtgagtgttt	ccctgtttcc	agccaagggg	101160
attgtgagtt	tctcctgggc	ctccttcaga	atctgggtgc	tctggaaagc	agtgttttgg	101220
caacatgggg	aaagtatggc	agtgtggggg	ggtcagctgg	gtctgggttt	gaatattgca	101280

tttgaatatt	ttaccagcat	tgatgtcgga	ttaaattattt	agtccctgta	agcctcagtt	101340
ttctcttctt	ctacatacac	ataatatatt	tgactctttg	ttgtgattat	tggttacaca	101400
tatgaagagc	ctggtgtggg	gcctggcaca	caataggtgc	tcaataaata	gaagttgata	101460
atttaattga	catgagtagt	agaaattatg	tccttgaaaa	caattgctgc	aagatagaag	101520
ttttcagcca	ggcacagtgg	ctcacatctg	ttgtaatccc	agcatattgt	gggggcccag	101580
gcggtatgaat	cacttgaggg	caggagtcca	agaccagcct	ggccaacgtg	gtgaaatccc	101640
ctctctacta	aaaatacac	tatttgccag	gcaggcgtgg	tgggcgacac	ctgtaatccc	101700
agctactgaa	gaggctgagg	cacaagaatc	gcttgaaccc	aggaggtgga	ggttgcagtg	101760
agctgagatc	actccactgc	attccagcca	gcgtgacaga	gtgagactct	gtctcagaaa	101820
aagaaaaaaa	agatagaagt	tttcttctgt	agatcagtgt	tagaactcat	accaagcgaa	101880
gtgggcctgg	tgagtatttc	agtgaaaaac	tgcatctctg	ctcagatatt	gtcaagactt	101940
ttcacccaaa	gattcttatt	tatgtctcag	tccgtacctt	gtgtgaaaat	taatactgga	102000
tgtcagaacg	ctgttgtgtt	tttaaagtcc	cctgggggta	agagcagttt	ccattaggtg	102060
ttctctgctt	tttacttaaa	aatcttactc	atgcattgag	caatatttat	tcagtctcta	102120
ttatgtgtca	ggtattttct	aggagctgga	ctcaactcaa	aagatatcct	tttgatgaga	102180
acaaagggtg	gtggatatat	gaaatattat	ctgtgggata	aatgcactta	gtcatgaggg	102240
agacttggtt	tgagtgccg	tcattgtatt	tgtactgttg	agttaacaac	ttctaggagg	102300
agctcagggc	cacttggcag	gggcttcttt	tgtcttgctg	ctcagcaagg	tgtattttgc	102360
tgtagagtgt	gctgggcagg	tgaacttttc	tttaactttct	cctgggtcct	tcctaaagca	102420
gcatgtacct	ttcccagagc	gaggagaggg	ccaccttctt	gtctcacaga	aacctccaat	102480
ctgttttgga	ctgcaggaag	gagccatagt	agtggaccag	caaatttttg	cccagagagat	102540
tgatttgctt	ccgattgtac	tttttttttt	tattgctact	ataacaagtc	accaataact	102600
tagcagttta	taaccacata	catttattat	ttcataaggc	cagaagccag	gatacagtag	102660
agctcaccta	ggtctacttc	ttagaggctc	acagggctga	tatcaagggtg	tttgtggggc	102720
tgtgtttttt	tggggggggt	ctgaagatga	atctgctttg	gagctcatcc	aggatatcag	102780
atgaattcag	tcccgtgcag	ttgtaggact	gaagtcctat	tccttgctgg	ctgtcagcag	102840
gggctgggtt	ttgctcctaa	agggtgccat	cattccttct	tatgcttttc	atgtgactcc	102900
tctcccacaa	gtgggttgag	tatctctcac	actttaaacc	tctgacgcct	cctgtcacat	102960
ctgtctccag	tcagagaaag	ttctttactt	ttaagggctc	agggtgttag	tttgggccc	103020
ttcacataat	ccaggataat	ctccttattt	tgagggttcat	aactttaatt	acatctacac	103080
agtgcatttg	ctatgaaatg	tgcatattca	cagactccag	gaataggggtg	tggacatctt	103140
tgcaagggat	attcagtctg	ctgtagcttt	ccttgattgga	aggaatagtt	tatcatatat	103200
ttgaagtgtt	ccctcagtgc	ttttggcttt	tgttgacccc	tctgcagctc	tctgcttttt	103260
cttgcccata	tttggaaggt	gactctaaag	cataataagc	atcacctatt	agggttttta	103320
atgtacaaac	caaacagagg	tgactttggg	aggagaacat	ctctgaacta	ggtatgagac	103380
attcatogaa	aaaaatccat	caagtgttta	ttgtatgtct	gctttatacc	agcactgttc	103440
taggcactga	agttcgacca	ccaacaaggc	agttgtgatg	cacttggagc	tttcattctg	103500
atgggcattg	agatccaggc	tgaaggctga	gtctgggaat	ttgaggaatt	ccttgttaggt	103560
cctgggtcta	cagagtgaga	gctgtcctcg	ttccagtttc	actgatgacc	tctcgaccag	103620
ctccctcaca	gcagtctttg	ccaacacaga	cactgtgggc	tgtagtggga	ggaatgtggg	103680
gttgaatgag	ctaggttttg	gctctgtcct	tgactcacca	ttgcctcagt	gatgtgaaaa	103740
tggtgtctga	tccttaagggt	tggaagtcca	ggcatgcaga	tttatctcca	tctcaataac	103800
gtggggaaaa	aaaagaagtg	gtttttgtgg	aaccagtggt	tccactgtcc	acgtgtcttc	103860
cagtgtgcct	agcacattcc	caccaagtgg	atcttgggtc	atgagggaaa	gaagggaaag	103920
tgaggggtgc	ccgaggctcc	cagaagacaa	gtaatgtcac	agctgagctg	tgtacagatc	103980
gaagaagcag	atggataagg	agtgaacaaa	gtcatccttg	tcttgagggg	tctttattta	104040
gcttcttctt	gactcttaga	caaggaccca	gaatacagat	ggggcttgtt	gttaccttca	104100
gcctcatggc	tttttagggc	tagatacttc	agcttgttac	atgcagtcct	taaagcgtct	104160
gtgtggggtt	ttgcaggaga	gaacacttgc	tctgtgtctc	ctgtctggaa	cccggacatt	104220
gttggaaggt	atcagatttt	gtttggcttt	gtgtgatttg	actgcccacc	tgtttacttg	104280
ctttctccca	gcaagcagcc	gcaatcccca	tgggttggtg	atgggtggaa	tgacacactg	104340
tgtagattta	ctcttcagac	tctatgttca	cctcattctt	atgggaaaag	aagagcacta	104400
gctggttagat	atagcagtg	gttaatatga	ctgtcgaact	ccatttacac	agacattttc	104460
accttagtta	tactatttct	tcattaaata	ttgttgccag	atctaagata	caggtttaat	104520

tttttctct	gaattatgtg	gtagtagatg	tattttaacta	tgttttagaaa	cagcaaaaaa	104580
tgaagcgttt	gaatgcgtta	aacacatcta	atgttgaaagt	taatatatttag	gttgtttgatt	104640
tatttttttaa	aagattagaa	tattccttag	aaatgtagtc	ttataatttc	gtattttcaat	104700
aaaaaatatt	aaaatgtttc	ccagaggaaa	tctttactgt	catagaaatc	accagaaaga	104760
gatagcaatt	actcctgggt	ggtagatgct	tttgatttgt	ggtttacttg	ttttcagttt	104820
gaactaaaa	atactaattcc	cagcctgagt	tggattttgc	atatgggtcaa	agtgaagtag	104880
agatttttgt	ctactttatg	aagatatatta	aaggacattt	gaaatgtttc	aatgaacaca	104940
ttgtaacatg	cattcccagg	aggaaaacaa	aattgtgtat	tgtgttgaaa	atactattcc	105000
aatatatgta	taccacagtc	tcattttgtc	atagaattcc	tgaaaaattt	agatgtagat	105060
gagatttttta	taagttgaaa	atatttttcag	ttgcatttta	attgcacaga	tgtgttttct	105120
acttctattt	ggctgtgact	cctaattgcat	tgtaatatta	tcttccagtg	ttcatttctgt	105180
gtagtgataa	tggattaaca	aatgcattca	ttcattttagt	aaacatttac	tgagccctaa	105240
tcagtgccat	gctctggccc	agggaggttag	tcattgtgcaa	ggtccagccc	tctctgtttc	105300
attcctgggt	ggggaatggg	tgggacagac	caggaaagga	gcagctgccg	tatagagcag	105360
gagacgctct	gctgggtgtg	atacagtcct	tgatggggcc	tcctactgca	gtctttccag	105420
tcaggaaaaga	aacatcctct	aagtggggac	ctaaagaatg	gatgtcagcc	aggtaaagaa	105480
cagggagtag	aatgttccag	gtagaggaca	tagtatatgc	attggtccag	agaggagagg	105540
gaagagaagg	tggcatttag	gggaactgta	cctgattgag	atagttcagc	atggagcaga	105600
tatagctgtg	gggagtttga	tgggagaagg	aacgatgaga	cgtgatgcct	gcagaggtgg	105660
gcaaaaggtcg	gctgaggcag	gtctttcttc	acgagccatg	tgaggatata	gggcttctac	105720
ctcagagtaa	agggagccat	taaaggctcc	acaggctgag	tgacttgatg	agggtgaatac	105780
gaaacagagc	atttctgtga	atgtgaatgg	cctttggagc	agaactaagt	tcattgaggat	105840
ggaaagaata	taatgaagcc	atctcttaga	cccagaaaga	atggggcaca	acagccttta	105900
tctttctggg	gccaatgtca	cagaatgcca	tgtcttttagg	aaacatggta	tgttgtgatt	105960
aacacatttt	gcagaagtgg	gtgggagctt	ttgaataata	acagtaagca	tttgtgcatt	106020
cttctgttaa	tgacattaca	gttatgatct	gaaaatattg	agtcatacat	gaattcctgt	106080
tatcttaact	cagaaaatat	agtccctcac	taaagggttt	attttccctc	tttttcccat	106140
ttcctttact	tcgtataaga	aagtcacttg	tctcctgggt	gcaatggaga	cctatgtgag	106200
ttcatagcca	agaaatggt	tttggttaga	aaaataatag	taggaattcc	aagctgtgaa	106260
ttttttactg	aagctctttg	gaaataggat	ttggcaagtt	ttgtctgcct	tcgtcaagta	106320
agcatgagca	ggagagcaca	gttaatagca	ggtgcagaca	catgattctc	agaccgtatt	106380
ttgtgttcta	gtttcaaggc	atgaattctt	tcctgggggt	aattttatcc	aaggaagtta	106440
tctgtctgtt	agatctgata	tgtgtctcagg	ccaacataga	ttcctttacc	ttcctttctt	106500
cctgtctcacc	tgctcttcc	cttttatctt	ttcattgaat	taaaaagaaa	attatgaaat	106560
agtttcaaca	tgaaaaaagg	tacagagaat	aacataaaga	acactcctgg	ctgggtgtgg	106620
tggctcacgc	ctgcaatccc	agcactttgg	gagtctgagg	cagccagatc	actggaggtc	106680
aggagtggga	gaccagcttg	gccaacatgg	tgaacactg	cctctactga	aaatacaaga	106740
attagccagg	catgggtggcg	tgcacttgta	atcccagcta	cgtgagagac	tgaggcagga	106800
gaattgcttg	aaccaggag	ggggaggttg	cagtgagctg	agatcacacc	actgcactct	106860
agcctgggtg	acagagttag	actcogtctt	caaacaaca	aacaaacaaa	aagaacactc	106920
ctgtaccatc	atccatcatt	ttgccgtgct	gactccaggt	tctattttaag	aaataaaaaca	106980
ttacaggtac	agctgatgcc	acctctgttt	ccctagctca	ttcttcagag	ataactcttg	107040
tcttgacgtt	ggatgtttta	atcctctata	tcantgtata	cttacattct	atgtataaca	107100
atatttggtg	ctggccctaaa	tgtgttcaca	ttgtataagt	gtgcatattg	gcttgccact	107160
tcattttgga	ttatgttctt	gagattttatc	aatgttgata	catgtggaat	ctgggttaatt	107220
tttgccatag	tattctattt	ttatactaaa	cttttaaaaa	tccatgcttc	tagtctttgg	107280
cttatttttt	caggttatgg	tatgtttttg	atgcacagaa	aagtaaaatt	aagtcattgag	107340
caaaatatct	ggataatcca	agcttttaaac	ttgatgtaga	atgtgaatca	tgtgtgtttt	107400
gttaaccctg	tgatgtcaat	ccatgcctga	ttgtgtaact	ccaaccaata	ttcctttgaa	107460
aatggaaatt	tgtttatatt	gactacagat	tgccaatatt	attagtaaat	gctgagcact	107520
taatctcgaa	taaagaacta	gttttaaaaat	gattctaaca	atggcattga	ctgttctacc	107580
ttattactca	tgggtgggtt	cagccaatgt	ttctgttgga	gacaaaaacc	aaaaacagtc	107640
aaattaaaca	agcagtcaaa	ccaacatac	agactactga	taagaaggtc	atatcataag	107700
atatggcatt	gaatttgtgt	ctgctaattg	aaaaatctga	tgcccacagc	aaacttaata	107760

aggacctatg	tttacatcca	tgctcaatta	cattcctggg	ttaaacagtc	atgcttttagg	107820
ccctgctgtg	tgccctggagt	tttgctgaag	tgtggggctt	ttaagagaag	gagaataaagc	107880
ttgctccaga	gttaagaaat	ttaaactaaa	agtcctaaag	atggttgaaa	aactattgccc	107940
cttgaagatg	taaattcatt	aagttggaga	agacctttta	tacaaacaac	agacccattc	108000
actgatttgt	acccttcagg	agacagatga	ccggtaattgg	tgacaatggg	tgaatggtgg	108060
gtttgggggt	tttagaaaca	tctgcacttg	gtgactactg	tatctaattg	gtgtgacaaa	108120
cctggcacc	catgtgtttg	gcaccatctt	gggtcctact	cagggccagg	tgaaccgagt	108180
ggcctcttca	ctgcttcaga	gtctgaagca	gattgtagta	tgccgaccag	acacagaata	108240
taccaccaag	cacgttggcg	caaagcatatc	tggaagggga	ggctttgtga	acatggtgct	108300
ggttctcaaa	cctcagtgct	caaaagagtc	tcctgaggat	tcctggatca	cactcttaaa	108360
cttctcattc	agtaggtgtt	agctggttga	gaatctgcat	tttttttttt	ttttctgaga	108420
ccgagtctca	ctctgatgcc	caggctggag	tgtattggcg	ccatcttggc	tcactgcaac	108480
ctctgcctcc	caggttcaag	caattttcct	gcctcagcct	ctctagtagc	tggtgattaca	108540
agcacatgcc	accatgcctg	gctaattttt	gtacttttag	tagagagggg	gtttcgccgt	108600
gttggccagg	ctcgtcttga	actcctgacc	tcagggtgatc	caccacattt	ggcttcccaa	108660
agtgttgaga	ttacaggtgt	gagccaccat	gccagcctg	aatctgcata	tttaacaagc	108720
accacaggtg	attctgatag	agtagctccc	caaacctcac	agtgttagtg	aatcccagtc	108780
atttacaatt	ctgccatgat	tttggtcata	ttcaagtga	gctggtagca	tttttagtta	108840
atatattttt	taaattaaagt	cacttctttt	ggataattaa	atttaattac	aaggggaagct	108900
ataccactgc	tgtaaaaaaca	tcacctgctt	ttaagagaag	gtacataatg	aatatacatt	108960
aagataaaga	tgtatatgtg	tgtgtgtgtg	cacatataag	tatacacata	cctaccatag	109020
ggattgagtt	ttccttcagg	tttttcaact	gaaatgtcaa	ctttgaggcc	agttaatatg	109080
tgtaagatat	atgtgtgtat	gtatgtctat	acatatagac	atatacgtaa	aaacatacat	109140
ggatgcatac	agtatatcta	tacacaacct	attatgcata	tcattgtatat	ttcatccact	109200
tagtattatc	ttnttatttt	gccgtttggc	aaatgctcag	taaaagaaaa	gggttagaag	109260
gggagaaagg	catttttatcc	caagccttca	ggaatcagga	tgaggatgtc	ttcaccttgt	109320
ggtggggagt	anattataca	attagagaca	gcacattgga	gntgtggctg	atatgctgtg	109380
tgatgatagt	cttagctctc	tgccatagcag	aggaaggaca	tttcaataga	agaaaaagtt	109440
taagaccttg	ccgagaaaca	gagaaaggat	gtttgtcttt	ttaagaagtt	gaaaaccctg	109500
tttgagacac	aaagccctcc	agttttggca	gtaaaacttc	atgcaaggga	agaaaaaggc	109560
aggggatgac	attgttgaca	attgtgagga	attaccatgt	gccaggcact	gtgagggggg	109620
ctttgtacat	atcctctagt	tttagtgctt	ataaaaaactc	tgtgatattg	gcacagccat	109680
ttaaactttg	ctgcatagtc	gagaaaaatgg	aaggatgggg	aatttgagtc	atttgcccag	109740
ggttctatag	ctacccacagg	ttcccatgac	tggaagaattg	gggcacaggg	tgccggggga	109800
gagtgaagtga	caagaatcct	aacaatctta	tttccattga	gtccttataa	aagaagtggg	109860
ttactacca	cgtttttaag	tttttcttaa	atttaggtta	tgtggatctg	gcgtttcttg	109920
ttttgtcctg	ggtttggttt	gtttttgcta	tgtgtcttg	aacatctgtc	atcttgtagg	109980
cctaaccgta	aacacaaaaa	cactttacct	cctatagctt	tcaattaaga	tctctcagtt	110040
tgtgtttgta	atagttttcc	aggcaagtcc	tccttaggtt	cggcttctag	tgtgttaacc	110100
tttagttata	aagtgaaccc	aaagagagaa	agtagaaaca	aaacacctca	cctgtttttg	110160
ctcatgaatt	actctctatg	gaaggaacaa	tcattgaacac	ctctgcgtat	cacagaggcc	110220
tatctgagtc	tgacgtttta	gggagaccgc	gtaggctcct	ttgaggactg	tgaatgtggg	110280
agtcctggga	ctctgggtgaa	gaaccctgtc	cagaagagat	gaatgagctg	gacaagttct	110340
ttcatagaac	cttttaggcag	gttttcttag	aaatgcacat	tgaggattat	gcttggtat	110400
tgtgatgatc	agaatgatac	tcaatccctt	ctgcatttgg	aattctcttt	gaaagaaaaa	110460
atcccaggca	gctattttctc	agagatagtg	agtcaccagc	acttctagac	attttcttgt	110520
gtagctctaca	ttataatttc	acagcagttc	ctgatatgac	aaatgtcaaa	atagcccaac	110580
cttctctaaa	cttcagagat	gtctgatatg	atattgaata	aaacaatgct	catagaaaca	110640
tcaagaaagg	tggattttcc	ctggatactt	ttttcctgct	tgacaaataa	cagtgaagaa	110700
actgatctca	cgtctttttc	tctttggaag	cctgaacact	cagaacccaa	cttgaggctc	110760
ctcagctata	gcaattctga	cttcacagtc	tgtaaaattat	tgttcttttt	tttcttttagc	110820
ttatgctttc	tgccctaatt	tatcttttcc	ctgttctaat	gaattattgt	cctatatctg	110880
ctgtgcagtt	aggtgacata	taacagcaat	taaatatatg	aattggtaca	tataaagatt	110940
tgactaaaaa	tcgatgtaaa	aataagtggt	ctacattcaa	tttccagttg	tagaaacagt	111000

gctgacttga	acagagtgc	agaattccat	ctttccctat	ttttgacagc	tttaaacttt	111060
atattttctt	cctttcttgt	gagccgcat	taacttttgt	tctcaaagnc	cattcccgtg	111120
ttacccatct	tgcagacgca	gacagatttg	ggaatttgcg	gtcagagttg	tattggacac	111180
atccccccag	cccacatgag	atccttttaa	tctattgcat	attaactagt	tttaagtaca	111240
atattctctac	ttcattttaa	accattaatc	aaagaatgag	tttgaaaatg	aacaaaatgc	111300
aaacttacag	ttagaaataa	ttgtagtgtc	tttagttttg	gttaggagtc	ggtttcttgt	111360
ttgttaaact	caagattgtg	aacagtttta	attcacttgt	ttatttccaa	tagagatttc	111420
agggtttacat	ttgaattcag	aaacaaagtt	ttctttctca	ttacagagaa	cactaaactc	111480
tacatctccc	ttcccagagc	aggagctggc	tgaagccaca	aaaacattgc	tgcatagtct	111540
tgggactctg	gcccaggagg	taagtgtgtg	ctttccagta	ccaggaagcg	gatcatccac	111600
tgtatcagta	ttttcattcc	tgagtctggc	aagaggtcct	tttgagttga	atatcacatg	111660
ggatgtaata	tcaattttca	aagtataagt	gatgtaaaaca	ataatgtttt	gatttccctta	111720
tttttagaaat	gaagaaacct	aaaactcata	gatgtctcag	agctaattgg	ttagtggcta	111780
acagctggat	atctagttta	gaacttttct	cattttttct	ttttgcccct	aggtaatccat	111840
acatttgtaa	agaggagaat	tatctctgcc	actgcccctg	cactgctttt	gtctgaccag	111900
caatttctcc	atattgcttc	ttcagtagca	aggccaatca	ttttaccaac	acacatgctt	111960
gctaactaac	aggaataacg	tggtaccctc	aattcagccc	tttcccttga	aagcatctgg	112020
cttctgaggt	tcaactatgg	gaatatggtc	tcttaatgaa	cattaagttg	agtttgccct	112080
ttagggtccac	atgttgacaa	atgtatcaga	gtaactctctg	tcctaggatc	agagggcctg	112140
taggcacttg	caaaagcagt	tagctctgac	tcccagccag	tgcaactccc	acctttctga	112200
ctcccagcct	tgtctcaaat	taggcttgga	agcgaggaac	tgtctgggtg	ccccagcat	112260
aggaagctga	gccagggggc	agtgtcaca	aacaatacag	actttaacgt	gtaggatatt	112320
ggaaaataat	aatttgtggg	gaaattgtct	cagacttggg	ccacccttat	ttttagctct	112380
ttctctaate	cgtttttctt	tttttgggtg	ttgtatctaa	cctaccattt	ttttgtgctt	112440
tgcatacttt	tttcaaatat	caaaaacgaa	ctttatgttt	tctaacaatg	aaagtattgc	112500
atgttcattg	tggaaaatgc	tgaagacttg	gaaaatacaa	aaatgctgag	atcaaacact	112560
attgatacgt	tagtgtattt	cttccctgtc	tgttctactt	tctttctttg	aattctgctc	112620
acgtgtttct	gactgatgag	gtctgacttt	tgggttccct	ttccagagga	gaagccttct	112680
ttcagcttgc	catttgttac	cctgggttatg	aaggctggta	acctttttta	ctaggtagag	112740
aagctggacc	aactgggggt	cttccagggg	gagaatgaga	aagagaaact	gttttgcaag	112800
tccgtagcta	tttctctagg	gccctgttag	ctgacattga	catgccttgc	attgctctgc	112860
agatccccct	gcagccctct	gtcccttgtt	catttctggc	cttagagaaa	gcaaaagcag	112920
gtctgtaaca	ggggaggctg	cctctaaact	cagggtttgg	ttacagctgt	tttcaactac	112980
atcactggcc	ctgggttttt	ttttttttct	ggcattaaaa	aaaaaaattg	gaagcagggtg	113040
atgttcccat	tgctgatgtg	gtggaaactc	tccaagtga	caatatacgt	ttttcttggc	113100
agctgtttct	tgtgccttgc	ttgtccttgg	tccaggacaa	gcaaggacca	tctgcctctt	113160
tcaatagaac	acctccagat	ccctttgatc	aaaagttact	cattgtctga	cttgctattt	113220
ctgtgagata	aatgggagaa	gatcaataaa	tgcacttgtt	tgtccagtca	gcngtgtgga	113280
aagttgataa	ttttgaccaa	agcacaaccc	ttgaaaggaa	aagaaaaagg	gagtgaatgt	113340
cttctgagaa	gctgcctagg	ttcagacagt	gtcacccatt	tccctgtatg	ctccacatga	113400
caaacctgag	tgggtctcat	catgtccatt	ttgcagatgg	caccaaggct	cagaaagggtt	113460
aggcaacttt	tccagtcacc	caatgagtta	attgacaaaa	ctgggattca	aaccagaaac	113520
tgttggattc	caaagcctgt	gttgttgcct	gottcgtgaa	aaactccagt	agcgactgga	113580
atagaaagga	gaaccttcca	agaaagaaaa	tacgcactag	cagaacctgg	aaattgggag	113640
gaaatgagga	cttgagggaat	aagatgaatg	aaagctgacc	tgagtttcac	atctgggtga	113700
tgggaaggga	ggacaggagg	gcagcatctc	agatgtccac	ccagcaccca	ccagctgcct	113760
ggcattgcta	ggtgttgagg	actcagcagt	gaacacgcta	acttctctgc	tttcttgggg	113820
cacgtatagg	gtgagagaca	gaaacaaaca	ggtcagtgtg	caatgccaca	ggagggatat	113880
atgcagtga	gaaaaagcag	ggtaaggggc	atagagcatg	agaagggtgt	ttttttaaag	113940
gggktgatta	ggaaaagctct	ctctaagggtg	acagttggac	ctgaaggaga	tgatagcatg	114000
tctgtgggtg	gggaaggaaa	ctccgaacag	gaagaatggc	agatacaaa	acattgatgc	114060
tagagcatgc	ctaagggaatg	tgtttaaggga	ccagggaaag	tgagcaagtg	gtggggggag	114120
gagaggagct	cagagcagga	ggaggtgagt	gccatacagg	cctggcaaga	ctttggattc	114180
ctgctgggtg	agatgagaat	ccagcggagg	gcttgaggga	ggggacatga	tgtgatctag	114240

agtttagact	gtttacactc	tggttggttg	gttgagaaga	gactgggatg	ggggaaaggg	114300
aggacaaagg	acattgtgct	ggattgagaa	agcagtaagt	cagtttcatt	cattcactca	114360
accgatgatg	ttcaaatacc	accatcatcc	gtgggctaaa	ggatgaagag	ccatccctcc	114420
ctgagagtca	ggaagcactt	cccagataaa	gtttggagtg	tgagctgagg	tgtagggagaa	114480
agagtaagag	tttacccttg	aaacgggtgc	tgggaaagagt	caatagtttg	gaataactca	114540
ataatattatg	gtgcttcttt	agaaagattt	gctggcttta	tgtgggaaga	aatttktttt	114600
tttgattggg	gagtggtggg	ttggtggtga	ggctgcctgt	ggaaagagaa	gtgagtggtt	114660
tgactcactg	ttatttaaaa	atctctaggg	ctgttccaat	aagcaacaaa	aggcaaaatg	114720
gcctggttct	ctgtcccttt	tctgtctgta	tgcctcgtag	aggttatgaa	aagaaaaagt	114780
tgggaaaagc	tgtccacctc	acctaattgt	gttcttggtg	agtgtgctag	atgccccctc	114840
tctggagaaa	aaaaatcctt	gtggcctctg	accacacctc	ggagagccta	gttcccttct	114900
ggaggcagaa	ggcaaagctt	aggacctaga	gagtgtctga	ccacgccact	cacaggaacc	114960
agcaggctgt	gaggttgaaa	gctaggcata	tgagcttttc	caggctgggt	gcagggcctc	115020
gtggcccttc	ccctcccttc	tgtgctctat	agctcagttc	tcccaggcgg	tgtgaacacg	115080
cagtgcacatt	tccaggaata	cagggattta	ttaatgattt	cttgtgaaat	gtttggaaat	115140
acaaagtact	ctataaatat	ttcataatag	cattggggct	gagaactcca	caaagtgccg	115200
gaatacattt	gcatgtaaga	cagaacgctg	cctgggtcat	tgatgcctgt	tgagtggcag	115260
tcacagacac	tgccatgggt	ttctgactca	cgctgttggg	actgttctat	gcagggcacc	115320
ctcttgtgtg	gcataggatt	tgtgcctcac	cacacactgt	tgtagctttg	ctgtcttgat	115380
gatgagtaga	gggcagtgct	caggccatgg	tataagcatc	tactgcccc	cagggttacc	115440
aaaaccaagc	caagttgtgt	ctcagcgagc	tccgtgaagc	atggagaagt	tgagtactca	115500
gagacatgac	gtgacttttc	aaaggctgta	agctgacgag	ggacatagct	agggttcaga	115560
cttgagtttt	tctttttctt	ttcttttttc	tttttttttc	aagactgagt	cttgcttttg	115620
tcgcccaggc	tgattgacag	tggtgcttgg	ctcactgcaa	cctctgcctc	ccgggttcaa	115680
gcaattctcc	tgccctcagc	tccccagtag	ctgggattac	aggcacctgc	caccatgcct	115740
ggccaacatt	tttgtatttt	tttagtagag	atggggtttc	accatgttgg	ccaggctggt	115800
cttgaactcc	tgacctcagg	tgatccaccc	gcctcgacct	cccaaagtac	tgggattaca	115860
ggtgtgagcc	actgcacccg	gcccagactc	gagtttttca	tcttaatgct	ttttcattgc	115920
ctgacacttt	actgagacca	agatagggaa	cttcacatac	agtacctttt	ctcccaaggc	115980
ggaagagggc	tgttcaattt	ctacactaga	gttcggggag	ttttagaaat	gagtcagtta	116040
tcgaggatga	gagcagttcc	tgataggctc	aaccacaatg	agatgtagct	gttcagagaa	116100
agcattcttt	tatctataaa	ctggaagata	atcccggtag	aacgaagccc	agccccaggg	116160
gcttcaactaa	ctccaggctg	tgcttctcaa	actttagtga	gcataggaat	cacctgggca	116220
tcttgtgaag	ctgtagattt	gaattctgca	ggtcggcaga	ggggtctcag	aatccgcatt	116280
tccaacaatg	tctccagtaa	tgctgatgct	gctcgtccct	ggaccacaga	ttgggtagcc	116340
aggttctggc	aagctcatcc	caaggctttg	agatgacatc	agacaaaata	tgttctggga	116400
catggctttt	gagaggtcaa	gaaaataaga	tgtttctttc	tcttctcatc	cccaaccctt	116460
gcaactgccct	tttctccctt	ccccaccctt	cctttctgtc	cccatccctg	acgccagctg	116520
ttcagcatga	gaagctggag	tgacatgcga	caggagggtga	tgtttctgac	caatgtgaac	116580
agctccagct	cctccaccca	aatctaccag	gctgtgtctc	gtattgtctg	cgggcacccc	116640
gagggagggg	ggctgaagat	caagtctctc	aactggtagt	aggacaacaa	ctacaaagcc	116700
ctctttggag	gcaatggcac	tgaggaagat	gctgaaacct	tctatgacaa	ctctacaagt	116760
gagtgtccat	gcagacccca	gcctgtctcc	caaccccatc	cctcccttag	ttctggcctt	116820
ggcctgtgtc	atctctctcc	tctgtagcag	cgttagatgt	ctacatgccc	atgtgcccac	116880
cagactgagc	tcttctctaga	ggagagaggc	ttctcttgaa	tagctacctg	tccccagttc	116940
tctgaatgca	gcctggcaca	tctcaggtgc	acagtagtgt	ttatcaatgg	aatgaatgat	117000
tgacagccaa	ccttctggtt	ttctggggga	tgtggaaggg	tggtctccag	ggtgatcaag	117060
aatgagataa	tggcagaagg	acaaatcctg	caagatctca	cttatatatg	gaatatatgt	117120
aaggtagaaa	gtgtcagttt	cacatgatga	ataagttcct	gggatcttga	tgtacatcgt	117180
gatgactata	gttagtaaca	ctgtatagta	tacttgaaat	ttgctaagag	gttagatccg	117240
aagtgttcac	actacacaaa	aaaggcaact	atgagggtgat	ggatttatta	acagcttgat	117300
tgtggtgatc	cttttacaaa	gtatcatat	attaaaacat	cacattgtat	accttaataa	117360
tatacaattt	ttatttgtca	gttgaaactc	aaaaaagcta	gaaaagcatt	tttaaaaaag	117420
atgatgtact	ggtcttaata	ttaccattga	gataagcttt	ataataacat	aaaaagaaat	117480

aacagtaatg	ataatagcaa	caacaacaac	aacaaagaac	taacatttaa	gtagaatttc	117540
ttgtgcactg	tgcatctctg	ttaagttatc	tcatttttacc	ctcatgataa	ccctgcaggg	117600
aagattcttt	aacccccacat	ttcataggtc	cagagaggtt	aagtgccttg	gttagagcca	117660
catcagagtt	aatccacaag	agccaggatt	caagcccaaa	tctgcctgga	tctgtgctct	117720
ctaagataac	tgtagtggt	ggcgtgtgtg	ttctcacact	cagacatttg	atctgccctt	117780
tgtttcccat	tcttagctgc	aaggcagtg	taaagaaccc	tggtgtctcca	tatccactcc	117840
ccacacttaa	gcacttttgt	gggcccgtgt	gccgtatgcc	tcgtggcagc	agggatccaa	117900
tgtcacagtt	ttaggcagtg	gcaccccttt	ccttgaaaac	ttgatgcagg	ggaacctttc	117960
tccatttcca	accacaggtg	tgctcnnttt	agacactgag	tgtaggcagg	ttttgtactt	118020
tattgtaaca	caagaacctt	ttcttctctg	gagtaaagca	ctccagacat	tcgcaagttg	118080
ctttacaagc	cttaaaagga	tggtattgta	ggcaacttta	attaaatccc	atctcctcct	118140
ctccccagc	ttgcaagttg	acccaaggaa	gccttcattt	ccatgacaga	cttaattgtg	118200
agggcatcct	cattaaaaaa	aaaaaaattc	tattatcttt	ccagcatata	gaagatactt	118260
ggtatctaaa	aatccctgaa	aaacttagaa	tgaattttta	aaaatcaggg	atcctgtctg	118320
ataaccaaac	ccatttgtct	gttacaactt	ttgtatttgg	gtttttgtta	agtgtacata	118380
tactagtttg	tgtaatttaa	agagaatttt	tttttttttt	tttgagaggg	agtctcgctc	118440
cggtgcccag	gctggagtg	agtggcgcca	tctcggtcca	ctgcaagctc	cgccctcccg	118500
gttcacgcca	ttctcctgcc	tcagccctct	gagtagctgg	aactgcaggt	gccccccacc	118560
atgccagct	aatttttttt	ttttttgtat	tttgagtaga	gacgggggtt	cactgtgtta	118620
gccaggatgg	tctcgatctc	ctgacctcgt	gatccgcctg	tctcggcctc	ccaaagtgtc	118680
gggattacag	gcgtgaacca	ctgcgcctcg	ttgagaattt	tttttttttt	ttttgggaga	118740
cagagtttctg	ctcttggtgc	ccgggctaga	gtgcagtgac	acaatctcgg	ctcactgcaa	118800
cctctgcctc	ctgggttcaa	gcgattctcc	tgccctagcc	tcatgcgtca	ccacgcccag	118860
ctaattttgt	attttttagta	gagacaggtg	ttctccatgt	tggtcaggct	ggtctcgaac	118920
tcccaacctc	aggtggttcg	cccgccttgg	cctcccaaag	tgctgggatt	gcaggcatga	118980
gccactgcgc	ccagccccaa	attttggttt	ttgcttgaaa	actgaggtct	gaattcagcc	119040
ttctggttgc	ccctcaagag	tcagtttaaa	tggtggtcat	gttagttgtc	agtgaataca	119100
atggtgaggg	tggcatgaga	gtgtgaatct	ggatgggagg	gcttgtgctt	catgaaaaca	119160
tttttccaga	tcagctcagt	cgtgagttat	ccgtcattga	cgttataata	agctctgatt	119220
atttatcaag	catcattctt	tatagatctc	tcagtttaat	ctgagataat	cttctccaca	119280
tctctccaca	tagatgttat	gaattttact	tttacagagg	agccaactga	ggctcagata	119340
agttacttat	tatatgacta	gtagtgttag	agctgggggt	tcaactaaga	actctctggc	119400
tccaaagccc	ttgtaagttt	ctatcagtat	atgaccatgc	atatgagcat	ttgtctctcc	119460
tcttcttcac	agctccttac	tgcaatgatt	tgatgaagaa	tttggagctc	agtcctcttt	119520
cccgcattat	ctggaaaagct	ctgaagccgc	tgctcgttgg	gaagatcctg	tatacacctg	119580
acactccagc	cacaaggcag	gtcatggctg	aggtaagctg	ccccagcccc	aagactccct	119640
ccccagaatc	tccccagaac	tggggggcaaa	aaactcaagg	tagcttcaga	ggtgtgcgct	119700
aagtatactc	acggctcttc	tgggaattccc	agagtgaaaa	cctcaagtct	gatgcagacc	119760
agagctgggc	cagctcccca	gtcgtgggta	tagaatcata	gttacaagca	ggcatttctt	119820
ggggatgggg	aggactggca	cagggctgct	gtgatggggt	atcttttcag	ggaggagcca	119880
aacgctcatt	gtctgtgctt	ctcctccttt	ttctgcgggtc	cctggctccc	cacctgactc	119940
caggtgaacc	agaccttcca	ggaactggct	gtgttccatg	atctggaagg	catgtgggag	120000
gaactcagcc	ccaagatctg	gaccttcctg	gagaacagcc	aagaaatgga	ccttgtccgg	120060
gtgagtgtcc	ctcccattat	taccatgtgc	ctgcttgata	ctggagaggt	gagtttctgg	120120
tcactttccc	aggtgtgagt	gaggtgagaa	ttctttcagt	ttatctagct	gggggaatgt	120180
agtgagcata	gctaaagtca	cagggcacca	cctctccaga	agtacaggcc	atggtgcaga	120240
gataacgctg	tgcatatcag	catccatgcc	actcacgggtc	aaatagcagt	tttctgcaaa	120300
acttagtgag	ggctgggtgt	tggaaagtga	gttgagtaat	tgcagtaccc	tattttcctt	120360
tttngctgca	gcctctcagc	cagccacagc	atctccctgt	gtcttggtag	gttttggaag	120420
gaagtgtggg	agcaaaagca	tgatgtttaca	tgtagactgg	cctgagatac	tcattctcag	120480
ggcactgtgt	gaatgatgag	ctgctgttac	tggtgtggagg	ggaaatgcac	ttagtgttcc	120540
agagccactt	gaaagggata	agtgtctctag	agacaaatgg	gttcaaatgt	ggagcaggct	120600
gagcaagaac	agaatgtctc	ctttgcctga	gcctgagtg	tgtaatcac	atcttctctg	120660
cttgggctga	gttagagaat	cattagacta	tttctgtttt	ccatggtgag	ggaggcctct	120720

tccttttgtc	tctgctcccc	ttaagaagca	ggtgaggatt	ttgccagggt	tcttgttttg	120780
aaccttattg	actttaaggg	cggctgggtt	ttagagactg	tacctacct	gggggaacac	120840
ttccgaaggt	taggactatt	ccctgatccg	ctgggaggca	ggttactgag	gaagtcctct	120900
taaaaacaaa	ggagtttata	ctgagaaaag	cataaacagt	gatttgtatg	gattcacact	120960
gactaatata	gctcatgcca	ttaaagtggg	gtctcttctc	taaaaggagg	ttatatgac	121020
tagccccgta	gacctaatg	tggtttcaga	cctgttcttc	ctggtcctct	ccttggaatc	121080
catatttcta	ctagttggac	tttttctgtt	tgtctggctc	tcagaggatt	ataggaggcc	121140
ctgtgaagtg	actcagtga	ttttgatttg	tgggcaagta	gatggttccc	tagtctgaaa	121200
ttgactttgc	cttaggtgct	tcaattcttc	ataagctccc	agttcttaaa	ggacaagatc	121260
cctgtaaaaca	tggcaatggc	attcattagg	aatctagctg	ggaaaatcca	gtgtgtatgc	121320
ttggaaatga	gggatctggg	gctggagaga	aaggcatggg	catgccttgg	agggacttgt	121380
gtgtcaagct	gaggaccttt	actttaagct	ctaggggacc	aggcaagggg	agatgtagat	121440
acgttactct	gatgggggtg	atgaattgaa	gaaggatgag	gcaagaatga	aggcagagac	121500
cagggaggag	gctctccaag	tggccaaggc	catcaaagtg	aaatgaggcc	tggtgactgc	121560
ttagtggcag	agcagtga	gagagggagg	gctactgagg	agtctcgatt	tctagctggg	121620
tgggtggtag	cgatgtccag	tagggccagt	tcagcctgtg	tctgcagtgg	aggagggtgg	121680
ttgggtcgga	gacagatgat	gagggagtc	tctttctctt	ggtggaagaa	aagggaaacct	121740
cttccaactg	ttttctttgc	ttcttccctc	tttttttttt	tttttttttt	tttggaacaga	121800
gtcttgctct	gtcaccaggg	ctgaaatgca	gtggcatgat	cctggctcac	cacagcctcc	121860
gcctcctggg	ttcaagcaat	tctcctgtct	cagcctccag	agtagctggg	attacaggca	121920
catatcactg	tgcccggcta	atttttgtat	ttcagtgga	gatgggattt	caccatgttg	121980
gtcgggtctg	aatgaactcc	tgacctcaag	tgatccacct	gcctcagcct	cccaaagtgt	122040
tgggattaca	ggcatgagcc	accgcccggc	gcctttcttc	cctctcttaa	agagtgttta	122100
tttaattcca	caaacatgag	cttgtcacc	cctgtagcct	ggcatctcct	acacgaggtg	122160
atggctgagg	cttctgcttc	tgtctgggta	gctctgatct	ttctgctttc	tctggcactg	122220
tctacccatg	ttgcctcacc	ccacaggtcc	cagggcacct	ctctcgggca	agtcttggaa	122280
ccctctgaca	ctgatttgct	ctcttttctg	agctgctttt	agccacccat	cctcgggacc	122340
tgttttctct	ctgcctccac	ccctgcccgc	agtcttaggt	ctcctgcccc	tcacgagcac	122400
cccagagagg	ccacgtgctc	agtcatctca	gtgggcgc	ctttctagtc	ttgctattct	122460
ttttggccat	gttggttcaga	aaccatactg	ggcagggccg	acttcaccct	aaaggctgcg	122520
tctcttcact	ctgcttttgt	ttgttccaaa	ttaaagtggc	tcagaattgc	taaccctagc	122580
ctctgtgaac	ttgtgaggt	caattttgtg	tctgttatgt	taacaaaaat	acatacat	122640
cttcctgggt	atggtataaa	ttgctattct	ctattggaaa	gcaatttggg	atgaaaattt	122700
aaagaacctat	tttaaaatat	gctatcctgc	gtacctccat	tcacccacc	cccagggatg	122760
tagcctactg	aaataatttt	aaagaagtca	ccatatgaga	gaaaatgtta	ttgctatatt	122820
gttattgtga	gaaattggaa	atagactaaa	tgttcagcac	tataggaata	attaatgaaa	122880
ttacatat	tctatacaat	cattatgctg	ccattgaaat	aataaaataca	aaggcgcaag	122940
gggggaaaag	cttataatgt	tagtgaaact	aagactgatt	tttttataaa	gcagcagttt	123000
tcagaccctt	ggagactcca	attcggtaga	accagagctt	catcttctct	gtcgaagctg	123060
tgacaggagt	tgcaaatgcc	tctccttttt	gctgagtttg	cagctgctgt	ttttccggca	123120
gcacatctgt	gcaggcctct	gcctcggccc	ctctggnatc	tgctgattga	gcagcggatt	123180
gatctgtcct	tctctttcgt	gttgacccat	gtgaggaacc	aactggcaag	ggaacaaga	123240
aatggaaaata	ggcctccttt	gcatcatgac	ctgtacatcc	tgcaattgga	aaagattgta	123300
ctttagttgg	tttaaccagc	agcattat	ttctaaacta	agcagtaaga	aggaattagg	123360
ttttatgtgg	gatcaacaga	ctgggtctca	aaagaggaag	gtgatagaac	acagtgggga	123420
gggggaggtg	cactagaaac	agagggccta	tgccttcatt	ctggctttgc	tacttaatag	123480
ctgtgtgacc	caatcttaga	gacttaacct	ctctgaactt	ccattttctc	atgtataaaa	123540
tgggaaatat	taaaggatac	tcactgggct	ggtggcttgt	gcctgtaatc	ccagcacttg	123600
gggaggttga	ggtgggagga	tcacttgagc	ccagggtgtc	aagaccagcc	caggcaacat	123660
ggcaagactc	tgtctctatg	aaaaaattaa	aaattagcca	ggtgtggtgg	tgtgcacctg	123720
tagtcttagc	tacttggtag	gctgagatgg	gaggatcact	tgggcttggg	aggtcaaggc	123780
tgcggtgagc	tgtgattcca	tcactgcact	ccagcccggg	cggcagagcg	agacactgaa	123840
tccaaacgac	aacaacaaca	aaaggcaaaa	aaataaaagt	gccctcttta	tggagttgtg	123900
taagggtgaag	catatacact	attcaacata	gtaactatat	aaaggaagta	ttgttgttgt	123960

tactgtagtt	aataccatta	agtgagatgt	ttcgtatagt	ggaaagcaca	tggaactctga	124020
attcagactg	gtctgacttt	gagtcctcagc	tccacatcta	gtaatactat	gaccaagccc	124080
tggttaaaat	catgtttttt	tttcttcagc	ctcagtcctc	tcacatataa	aatagggaca	124140
ctgtcattta	cctcagtttt	ctgtgaggat	aaaacaacga	cagtgtatat	gcaagtattt	124200
tgtaaatttt	gtagtgtcc	tcaagattta	gttggtgttt	actacttgta	ctttctcact	124260
ggaatggcag	atgctgttgg	acagcagggg	caatgaccac	ttttgggaac	agcagttgga	124320
tggttagat	tggaacagccc	aagacatcgt	ggcgtttttg	gccaaagcacc	cagaggatgt	124380
ccagtccagt	aatggttctg	tgtacacctg	gagagaagct	ttcaacgaga	ctaaccaggc	124440
aatccggacc	atatctcgct	tcatggagggt	gaatctgttg	ctgggatcat	ttagaaaaga	124500
cttaacggct	tctttctctg	agacgtttaca	ataaggttca	ggcaggaggc	aagtttagaa	124560
ataatgtata	gtctcattta	caaaactatc	cctcaagcct	aacacaggat	ttgataacaa	124620
aaggcactta	ataaatgtta	gttgagtgggt	tgaatgagta	aataaaactct	agcttttagta	124680
aattaaactct	agcttattct	atataggctc	aagagaatat	ttctacccat	tttcttctag	124740
gttttcctat	ctcagtgact	aatggtagca	aagcattccc	ttaaaaaggc	attatttgtg	124800
aaacttatct	aaaatcgaat	tccgggtccaa	ttaaattttt	gaaattttat	attaaaaatt	124860
atattagtag	ggatgggtaa	gaggtgtttt	ggtctgggtg	gttggttagt	tgctatgact	124920
cagaattgct	aagaaaacag	aaaagtaaga	taagatcatt	gttttaacct	cttttcctcc	124980
acaaaaatcaa	taaataacat	atccctaaat	tactcttaga	atttctctta	aattgcagtg	125040
aaaaaccaa	atccttcatt	cttggttgaa	ggttggaata	ctacgttaga	gaggattaga	125100
gagagaggat	gagcaatcgt	gtagtcagcc	cttgccctct	agtgtaggat	ttgtctcagc	125160
cactgcttgt	tgctctggct	gccaacgttc	tcatgaaggc	tgctcttcta	tcagtgtgtc	125220
aacctgaaca	agctagaacc	catagcaaca	gaagtcgtgc	tcatacaaca	gtccatggag	125280
ctgctggatg	agaggaagtt	ctgggctgggt	attgtgttca	ctggaattac	tccaggcagc	125340
attgagctgc	cccatcatgt	caagtacaag	atccgaatgg	acattgacaa	tgtaggagag	125400
acaaataaaa	tcaaggatgg	gtaagtggaa	tcccatcaca	ccagcctggg	cttggggagg	125460
tccagagcac	ctattatatt	aggacaagag	gtactttatt	ttaaactaaa	atttggtaga	125520
aatttcaaca	acaacaaaaa	aactcaactt	ggtgtcatga	ttttggtgaa	attggtacat	125580
gacttgctgg	aagggttttc	ataggtcata	aaataacagt	atcttttgat	ttagcatttc	125640
tactcaaggg	aattaattcc	aggaattttg	gtggcaggca	cctgtaatcc	cagctactcg	125700
ggaggctgag	gcaggagaat	tgcttgaacc	caggaggcag	aggttgacgt	gagctaagat	125760
cgcacattg	cactcccgc	tgggcaataa	gagtgaaact	ccatctcaaa	aaaaaaaaaa	125820
gatacaaaaa	tagaaaaagg	ggcttggtta	gggtagtagg	gttttgggca	attttttttt	125880
ttttttttt	ttttattgta	tggttctaaa	ggaatgggtg	attacctgtg	gtttgttttt	125940
aggtactggg	accctgggtc	tcgagctgac	ccctttgagg	acatgaggta	cgtctggggg	126000
ggcttcgct	acttgaggga	tgtgggtggg	caggcaatca	tcagggtgct	gacgggcacc	126060
gagaagaaaa	ctgggtgtcta	tatgcaacag	atgccctatc	cctgttacgt	tgatgacatg	126120
taagttacct	gcaagccact	gtttttaacc	agtttatact	gtgccagatg	gggggtgata	126180
tatgtgtgtg	catgtgcatg	catgtgtgaa	tgactctggaa	ataagatgcc	agatgtaagt	126240
tgtcaacagt	tgcagccaca	tgacagacat	agatatatgt	gcacacacta	gtaaacctct	126300
ttccttctca	tccatgggtg	ccacttttat	ctttttattt	ttattttttt	ttttgagatg	126360
gagtcctcgct	ctgacgcccc	ggctggagtg	cagtggctcg	atctcggtct	actgcaacct	126420
ttgcctcccg	ggttcaagct	attctcctgc	ctcagcctcc	acagtacgtg	ggactacagg	126480
ctcatgctgc	cacgcccggc	tgactttttg	tatttttagta	gagacgaggt	ttcaccatgt	126540
taccaggct	agacttcaac	tcttgagctc	aggcaatcca	ccctccttgg	cctcccaaag	126600
tgctgggatt	acagggtgtga	gccactgcac	ccagcccacc	actttaattt	tttactctct	126660
acccttttgg	tcaaaatttg	ctcaatctgc	aagcttaaaa	tgtgtcatga	caaacacatg	126720
caagcacata	ctcacacata	gatgcagaaa	cagcgtctaa	acttataaaa	gcacagttta	126780
tgtaaatgtg	tgcacttctt	ctccctaggt	ggtaaaaccac	atttcaaaac	aacccaaata	126840
aaactgaaca	aagcttcttc	ctcttagact	ttttagaaaa	tctttcagtg	ctgagtcact	126900
aagctgccaa	gttctcattg	tgggaactat	gcctttggat	gtaatgattt	cttctaagac	126960
aatggggcga	ggtgtagtta	ttgcagacat	ctgaaatatg	taatgtttct	tccagattct	127020
ggaaattctc	ttattctctg	tggttggtgg	tggttggtgg	atgtgtgtgt	gtgtgtgtgt	127080
gtgtgtgtgt	gtgtgtgtgt	agggatcagg	atgcgggagg	agctgggttc	tgcttgtatt	127140
ggttctctgt	tttgcattga	atagtggtgt	tccttgtagt	gctatctata	gcttttcaag	127200

gtcaccagaa	attatcctgt	ttttcacctt	ctaaacaatt	agctggaatt	tttcaaagga	127260
agactttttac	aaagaccctt	aagctaaggt	ttactctaga	aaggatgtct	taagacaggg	127320
cacaggagtt	cagaggcatt	aagagctggg	gcctgttggt	atgtagttag	tatgtgccta	127380
catggtaaaag	ctttgacgtg	aacctcaagt	tcagggtcca	aaatctgtgt	gcctttttac	127440
tttgacatc	tgcattttct	attctagctt	ggaatctgaa	acattgacaa	gagctgcctg	127500
aaatgtatgt	ctgtgggtgt	attagagtta	cgataagcaa	gtcaatagt	agatgacctt	127560
ggagatgttg	aactttttgt	agagaatgag	ttgttttttt	gttttggttt	ttagtacttt	127620
aacataatct	accttttagt	taagtatcgc	tcacagttac	ctagttactg	aagcaagccc	127680
ccaaagaaat	ttggtttggc	aacactttgt	tagcctcggt	tttctctcta	cattgcatgt	127740
ctcgtgaagc	attggatcat	acgtacattt	cagagtctag	agggcctgtc	cttctgtggc	127800
ccagatgtgg	tgctccctct	agcatgcagg	ctcagaggcc	ttggcccatc	accctggctc	127860
acgtgtgtct	ttctttctcc	ccttgctcct	ccttggggcc	tccagcttcc	tgcgggtgat	127920
gagccgggtca	atgcccctct	tcatgacgct	ggcctggatt	tactcagtg	ctgtgatcat	127980
caagggcatc	gtgtatgaga	aggaggcacg	gctgaaagag	accatgcgga	tcattgggct	128040
ggacaacagc	atcctctggg	ttagctgggt	cattagtagc	ctcattctcc	ttcttgtgag	128100
cgctggcctg	ctagtgggtca	tcctgaaggt	aaggcagcct	cactcgcctc	tccttgccag	128160
gaaactccga	aatagctcaa	cacgggctaa	gggaggagaa	gaagaaaaaa	aatccaagcc	128220
tctggtagag	aaggggtcat	acctgtcatt	tcctgcaatt	tcattccatt	atagttgggg	128280
aaagttaggc	ccagagaggg	gcagtgactt	gccccaggtc	aaccagcccg	ggtagcagct	128340
aagtaggatg	agagtgcagg	gttcatgctt	tccagataac	cacatgctca	actgtgccat	128400
gctgtctcat	tggtagtggg	tcattggcagc	atctgaaagc	tatttatttt	cttagatata	128460
ttgggtggcg	attcttctta	agtttctaag	aacaataatc	agaaggatat	atattgttgc	128520
aggtttagact	gtctggaagc	agaggctgaa	atagagtttg	atgtatgggt	atttatgagg	128580
gctcaatacc	tatggaagag	atatggaaga	tgaggagatt	ggcagaggga	ggagttgaac	128640
tgtgatatag	ggccaacccc	gtggggcact	ctagagaata	tgagccttgt	tggtgtgtgt	128700
cttcacagag	ctgaaacatc	cagccccttg	tgctccccc	aggcctccct	cctgacacca	128760
cctacacag	ccctctcaat	caatcactgg	atgtgggctg	ccctgggaag	gtcgtgcccc	128820
aggccctaca	tggtctctct	ctgctgtgac	aaaccacag	ttgctgatgc	ctgaggccgt	128880
ctactgacag	ctgggcaaca	aggcttcctt	gaatggggac	tctgggcagt	gcagttttgt	128940
gtctgaacca	tacattaata	tatttatatc	cgaattttct	ttctctgcaa	gcatttcata	129000
taaagacaca	tcaggtaaaa	ataaatgttt	ttgaagcaaa	aggagtacaa	agagataaga	129060
actaactaat	tttaatactg	ttaccactct	ttacaaatag	ttcctactga	ttgccaagga	129120
ctgttttaac	acatcacatg	ggcttcttct	tctatcctca	ctaacccttt	taacagacaa	129180
ggaaatgagg	ctcaggaagg	tcaaggactt	tattgagggt	ccacagtagg	atacagttct	129240
tgctaaaagc	aacccctccc	tcattgctctg	ttatctaact	gcaaggggaa	ggtcagtggt	129300
agaggtagtg	gtcccatggg	tggtgcataa	gagctgctct	gagacaactg	catgctgggt	129360
ggctcctgcag	acatgtacct	atcagccgga	gataggctca	aaatatccac	aagagtttgg	129420
atgattgtgg	gaatgcagaa	tccatgggtga	tcaagaggga	aagtcaagtt	gcctggccat	129480
tttcccttggc	tttttagacag	aaaagttacg	tggtgatatta	tctcccacag	ctcttctgtg	129540
gtgccaccag	tcattagtcct	tatataagga	gaaaccagtt	gaaattacct	attgaagaaa	129600
caaaagacaa	actcgccccc	tgaaatgcgt	agaaagccct	ggactctgtt	gtattcataa	129660
ctctgccatt	atttttctgc	gtagttttgg	gtaagtcact	tatcttcttt	aggatggtaa	129720
tgatcagttg	cctcatcaga	aagatgaaca	gcattacgcc	tctgcattgt	ctctaactg	129780
agtaggaata	aacccctgtct	tttttctgta	gatcatacaa	gtgagtgtct	gggattgttg	129840
aggcagcaca	tttgatgtgt	ctcttctctt	ccagttagga	aacctgctgc	cctacagtga	129900
tcccagcgtg	gtgtttgtct	tcctgtccgt	gtttgctgtg	gtgacaatcc	tgcagtgtct	129960
cctgatttagc	acactcttct	ccagagccaa	cctggcagca	gcctgtgggg	gcattcatcta	130020
cttcacgctg	tacctgccct	acgtcctgtg	tgtggcatgg	caggactacg	tggtgttcac	130080
actcaagatc	ttcgctgtga	gtacctctgg	cctttcttca	gtggctgtag	gcatttgacc	130140
ttcctttgga	gtccctgaat	aaaagcagca	agttgagaac	agaagatgat	tgtcttttcc	130200
aatgggacat	gaaccttnag	ctctagattc	taagctcttt	aagggttaagg	gcaagcattg	130260
tggtttatta	aattgtttac	ctttagtctt	ctcagtgaat	cctgggtgaa	ttgaattgaa	130320
tggaattttt	ccgagagcca	gactgcatct	tgaactgggc	tggtgataaa	tggtcattgag	130380
gaatggcttc	aggcaacaga	tgccatctct	gccctttatc	tcccagctct	gttggctatg	130440

ttaagctcat	gacaaagcca	aggccacaaa	tagaactgaa	aactcttgat	gtcagagatg	130500
acctctcttg	tcttccttgt	gtccagtatg	gtgttttgct	tgagtaaatgt	tttctgaact	130560
aagcacaact	gaggagcagg	tgccctcatcc	cacaaattcc	tgacttggac	acttccttcc	130620
ctcgtacaga	gcagggggat	atcttggaga	gtgtgtgagc	ccctacaagt	gcaagttgtc	130680
agatgtcccc	aggtcactta	tcaggaaagc	taagagtgc	tcataggatg	ctcctgttgc	130740
ctcagctctgg	gcttcatagg	catcagcagc	cccaaacagg	cacctctgat	cctgagccat	130800
ccttggctga	gcagggagcc	tcagaagact	gtgggtatgc	gcatgtgtgt	gggggaacag	130860
gattgctgag	ccttggggca	tctttggaaa	cataaagttt	taaaagtttt	atgcttcact	130920
gtatatgcac	ttctgaaatg	tttgtatata	atgagtgggt	acaaatggaa	tcattttata	130980
tgttacttgg	tagccaccca	ctnccctaaa	gggactctat	aggtaaatac	tactcttgca	131040
ccttatgatt	gateccatttt	gcaaattcaa	atttctccag	gtataattta	cactagaaga	131100
gatagaaaaa	tgagactgac	caggaaatgg	ataggtgact	ttgcctgttt	ctcacagagc	131160
ctgctgtctc	ctgtggcttt	tgggtttggc	tgtgagtact	ttgccttttt	tgaggagcag	131220
ggcactggag	tcagtgagg	caacctgttt	gagagctctg	tggaggaaga	tggcttcaat	131280
ctcaccactt	cgggtctccat	gatgctgttt	gacaccttcc	tctatggggg	gatgacctgg	131340
tacattgagg	ctgtcttttc	aggtagactg	ctttgggcat	ctgtttggaa	aatatgactt	131400
ctagctgatg	tcttttcttt	gtgctagaat	ctctgcagtg	catgggcttc	cctgggaagt	131460
ggtttgggct	atagatctat	agtaaacaga	tagtccaagg	acaggcagct	gatgctgaaa	131520
gtacaattgt	cactacttgt	acagcacttg	tttcttgaaa	actgtgtgcc	aggcagcatn	131580
gcaaaatggt	ttatacacat	tgcttcattt	aattctcaca	aggcntactn	ctgaagtagt	131640
tactataaata	accagcaatt	ttcaaagtga	agaactgtga	ctcaaagacg	ttaagtaacc	131700
agctttgggtc	acacaactgt	taaatgttgg	tacgtggagg	tgaatccact	tcggttacac	131760
tggttcaata	agcccaggcg	aatcctccca	atgctcacc	aattctgtat	ttctgtgtcc	131820
tcagaggggg	tacaactagg	agaggttctg	tttcttgagt	acaggttgtt	aataattaaa	131880
tatactagct	ctaaggcctg	cctgtgattt	aattagcatt	caataaaaaat	tcattgttga	131940
tttttcttta	gtacttcttt	cttaatatata	tacatcttct	tgaccaagtc	caagaggaac	132000
ctgcgttggg	cagtttttcat	atgagatcaa	attcttgagag	agcaagattt	aacccttttt	132060
ggttcacctt	ctgatctctc	cctaaggagg	tatacatgaa	atattttatta	ctcctgcctg	132120
aacttctttc	attgaatatg	caatttttga	gcatgcagat	tctggattta	aattctgagt	132180
cttaacttac	tggttgaggg	accttggata	ggctccttat	ccctcagttt	cctcatctct	132240
aaaatgggga	tggtcacctgc	cccggtgggt	gttgggaagg	cttacagagg	tgcagaatgt	132300
acgttgtaca	tagcaggttt	cagcaaatgt	tagctccctc	tttccccaca	ttccattcaa	132360
tctgttcttt	ctccaaagga	tgtgtcaaag	aggaaatgga	cctgggtggg	aaaccttcag	132420
aatactggga	tgatgctgag	cttggctcat	acctgtgctt	tgctttcagg	ccagtacgga	132480
attcccaggc	cctgggtattt	tccttgcacc	aagtcctact	ggtttggcga	ggaaagtgat	132540
gagaagagcc	accttggttc	caaccagaag	agaatatcag	aaagtaagtg	ctggtgacct	132600
cctgctcttt	ctttaacctc	gtgctgtgc	ctctgtcaac	tggtgggggc	aagcgatgtc	132660
tcctgccttt	ctaaaagact	gtgaaaccac	tccaggggca	gagaaatcac	atgcagtgtc	132720
cctttccaaa	tcttcccatg	ccatttatgt	ccaatgctgt	tgacctattg	ggagttcacg	132780
gtctcgatcc	ctgagggaca	ttttctttgt	tgtcttggct	tctagaagag	tatcttttac	132840
ttgccccctc	ccaaacacac	atttcatggt	ctcctaacaa	gctagaagaa	agaggtaaaag	132900
acaagcgtga	ttgtggaacc	atagcctcgc	tgcttgcctg	tgacatgggtg	acctgtgtat	132960
cagcctgtgt	gggctgagac	caagtggcta	ccacagagct	cagcctatgc	ttcataatgt	133020
aatcattacc	cagatcccta	atcctctctt	ggctcttaac	tgacagacaga	gatgtccaca	133080
gctcatcaaa	ggctctgcct	tctgggttct	ttgtgcttag	agtggcttcc	ttaaatttta	133140
ataggtccct	tttctgccag	tctcttctgt	gccccctccc	tgattgccct	tggtaaaagt	133200
atgatgcccc	ttagtgtagc	acgcttgcct	gctgttccca	atcatcttct	cctacctcct	133260
ctttacacct	agctcctgtt	tcagtcacct	agaaatgctc	acagtcgctg	gaatatgtca	133320
tgttcttcca	cacctccatg	cctttgtagg	tactgtttgc	tctcacagga	gaactttctc	133380
tctaacttgc	ctatcttctc	aactcctcct	ttctctccaa	gatctagtcc	cggatccccct	133440
cccctgagca	tcctccttgc	gttctcaggt	agtcagtcac	tctctgcccc	gaacttccat	133500
ggcacgtgaa	agaaaatctt	tttattttaa	aacaattaca	gactcacaag	aagtaataca	133560
aattacatga	gggggttccc	ttaaaccttt	catccagttt	ccccaatggg	agcagcatgt	133620
gtaactgtag	aatagtatca	aaacctgtaa	attgacatag	gtacaattca	caaaccttct	133680

tcagatttca	ctagctttat	gtgcgctcat	ttgtgtgtgt	gtgtgcgtat	ttagttctat	133740
gcaattttat	catgtgtgaa	ttcatgtaat	tactagctca	gtcaagctgc	agaaatatct	133800
cattgtcaca	aagctccttc	atgctacccc	ttaantggcc	acnagccnac	ctcccttctt	133860
cctcagttcc	tgacacctgt	caaccactaa	tgcgttcctc	gtttttacag	ttttattatt	133920
tctagaatgt	tacataaatg	gaaccatata	gtaggtatcc	ttttgatact	ggcttttttt	133980
tttttttcac	tcagcagtat	tcccttagat	ctatccaagt	tgtgtgtgtc	aacagttcat	134040
tcctcttcac	tgctgagtag	tgttccctgg	gaggggtgta	tcacagttcc	atggcatttt	134100
tagatgtatt	ttttaaacag	ctttcagcat	cctctatttt	aattgttcat	caagtccttt	134160
ttcccaatag	actctgaatg	ctcctttatc	atcgatttcc	catcaccaac	atcagtatcc	134220
aaataggccc	tataataaca	tttatagcct	cctgcctgcc	tgagaaacca	gggtggacat	134280
ggagagaagg	cacttctgaa	agttcaagcg	cagtgcactg	tgtccttaca	ctccactcct	134340
cagtgtcttc	tgtgggttca	ttctgtctct	ctctcctgtc	acagtctgca	tggaggagga	134400
accacccac	ttgaagctgg	gcgtgtccat	tcagaacctg	gtaaaagtct	accgagatgg	134460
gatgaagggt	gctgtcgatg	gcctggcact	gaatttttat	gagggccaga	tcacctcctt	134520
cctggggccac	aatggagcgg	ggaagacgac	caccatgtaa	gaagaggggtg	tggttcccg	134580
agaatcagcc	acaggaggggt	tctgcagtag	agttagaaat	ttatacctta	ggaaaccatg	134640
ctgatccctg	ggccaaggga	aggagcacat	gaggagtgtc	cgaatgtgaa	catgttatct	134700
aatcatgagt	gtctttccac	gtgctagtgt	gctagatgtt	atttcttcag	cctaaaacaa	134760
gctggggcct	cagatgacct	ttcccatgta	gttcacagaa	ttctgcagt	gtcttggaa	134820
ctgcagccac	gaaaagatag	attacatatg	ttggaggag	ttggtaatc	ccaggaactc	134880
tgtctctaag	cagatgtgag	aagcacctgt	gagacgcaat	caagctgggc	agctggcttg	134940
attgccttcc	ctgcgacctc	aaggacctta	cagtgggtag	tatcaggagg	ggtcaggggc	135000
tgtaaaagcac	cagcgttagc	ctcagtggct	tccagcacga	ttcctcaacc	attctaacca	135060
ttccaaaggg	tatatctttg	gggggtgaca	ttcttttctt	gttttctttt	taatcttttt	135120
ttaaaacata	gaattaatat	attatgagct	tttcagaaga	tttttaaaag	gcagtcagaa	135180
atcctactac	ctaacacaaa	aattgttttt	atctttgaat	aatatgttct	tgtttgtcca	135240
ttttccatgc	atgcgatgtt	aggcatacaa	aatacatatt	ttaaagaata	ctttcattgc	135300
aaattggaaa	cttcgtttaa	aaaatgctca	tactaaaatt	ggcatttcta	acccataggc	135360
ccacttgtag	ttattttaccg	aagcaaaagg	acagctttgc	tttgtgtggg	tctggtaggg	135420
ttcattagaa	aggaatgggg	gcggtgggag	gggtgtgtgt	ctgttctctc	tgcagactga	135480
atggagcatc	tagagtttaag	ggtaggtcaa	ccctgacttc	tgtacttcta	aatttttgtc	135540
ctcaggtcaa	tctcgaccgg	gttgttcccc	ccgacctcgg	gcaccgccta	catctctggg	135600
aaagacattc	gctctgagat	gagcaccatc	cggcagaacc	tgggggtctg	tccccagcat	135660
aacgtgctgt	ttgacatgtg	agtaccagca	gcacgttaag	aataggcctt	ttctggatgt	135720
gtgtgtgtca	tgccatcatg	ggaggagtgg	gacttaagca	ttttactttg	ctgtgttttt	135780
gttttttctt	tttttctttt	ttattttttt	gagatggagt	ctcgtctctg	agccaggctg	135840
gactgtagt	gcgcgatctc	ggctcactgc	aaccttggcc	tcccagggtt	aagcgattct	135900
cctgcctcag	cctcccgagt	agctgggact	ctaggcacac	accaccatgc	ccagctaatt	135960
tttgtgtttt	tagtagagac	gggttttcac	catgttggcc	aggatggtct	caatgtcttg	136020
acctcgtgat	ccgcccacct	cggctctcca	aagtgtctgg	aacacaggca	tgagccactg	136080
tgtctggcca	cattttactt	tctttgaata	tggcaggctc	acctccgtga	acaccttgag	136140
acctagtgt	tctttgattt	taggagaagt	gggaggtgaa	tggttgagct	gtagaggtga	136200
catcagccca	gccagtggat	gggggcttgg	gaaacattgc	ttcccattat	tgtcatgctg	136260
gagggccctt	tagcccatcc	tctccccccg	ccacctcct	tattgaggcc	tggagcagac	136320
ttcccagacc	tggtagtgtc	tcagggccct	ggtatgatgg	acctataatt	gctgcttaag	136380
acatttgctc	ccactcaggt	tgtcccatca	gccataaggc	ccccagggag	cccgtgtgat	136440
ggagcagaga	gagacctgag	ctctgcaatc	ttgggcaagg	cttttccctt	atgtttcttc	136500
ttatctaaag	tgaacagctg	gggctcatgt	gctccctcct	catctaaagt	gaacacatgg	136560
ggctcatgtg	cagggtcctc	cccgttttca	gagcctgagg	tcccttgagg	ctcaggaagg	136620
ctgctccagg	tgagtgccga	gctgacttct	tggtggacgt	gctgtgggga	cagccatta	136680
aagaccacat	cttggggccc	tgaaattgaa	agttgttaact	gcctgggtgca	tggtggccag	136740
gcctgctgga	aacagggttg	aagcgatctg	tcacctttca	ctttgatttc	ctgagcagct	136800
catgtggttg	ctcactgttg	ttctaccttg	aatcttgaag	attatttttc	agaaattgat	136860
aaagtatttt	taaaaagcac	ggggagagaa	aaatatgccc	attctcatct	gttctggggc	136920

aggggacact	gtattctggg	gtatccagta	gggcccagag	ctgacctgcc	tccctgtccc	136980
caggctgact	gtcgaagaac	acatctggtt	ctatgcccgc	ttgaaagggc	tctctgagaa	137040
gcacgtgaag	gcgagatgg	agcagatggc	cctggatggt	ggtttgccat	caagcaagct	137100
gaaaagcaaa	acaagccagc	tgtcaggtgc	ggcccagagc	taccttccct	atccctctcc	137160
cctctcctc	cggctacaca	catcgaggag	aaaatcagca	ctgccccagg	gtccccaggct	137220
gggtgcggtt	ggtaacagaa	acttgtccct	ggctgtgccc	ctaggtcctc	tgcttccact	137280
cactgtctgg	ggctggctct	ggagtttgct	ttgctctggt	tttttgtagg	tggaatgcag	137340
agaaagctat	ctgtggcctt	ggcctttgtc	gggggatcta	aggttgtcat	tctggatgaa	137400
cccacagctg	gtgtggaccc	ttactcccgc	aggggaatat	gggagctgct	gctgaaatac	137460
cgacaagggtg	cctgatgtgt	atttattctg	agtaaatgga	ctgagagaga	gcgggggggct	137520
tttgagaagt	gtggctgtat	ctcatggcta	ggcttctgtg	aagccatggg	atactcttct	137580
gttakcacag	aagagataaa	gggcattgag	actgagattc	ctgagaggag	atgctgtgtc	137640
tttattcatc	tttttgctcc	caacatgggtg	cactaaatct	atgggttagt	gaaaggggtg	137700
atgcttaaat	gaatggaagc	ggagaggggc	aggaagacga	ttgggctctc	tggttgaggc	137760
tctgatgtgg	tacagtatga	ggagcacagg	caggcttggg	gccaactctg	gcntggccct	137820
gagacattgg	gaaagtcaca	acttgccctc	ccttctttgc	cgataataat	agtgggtgct	137880
tacctcatag	aggattaaat	taaatgagaa	tgacacacaa	ccacctagca	caatgcctgg	137940
catatagcaa	gttcccaaat	aaaatgcnta	ctgttcttac	ctctgtgagg	atgtggtacc	138000
tatatataca	aagctttgcc	attctagggr	tcatagccat	acagggtgaa	aggtgggcttc	138060
caggctctct	ccagtgtcta	cccctgtcta	tatctctcta	gtccctgtca	ctgtgacaaa	138120
tcagaactga	gaggcctcac	ctgtcccaca	tccttggtgt	tgtgctgggc	aggccgcacc	138180
attattctct	ctacacacca	catggatgaa	gcggacgtcc	tgggggacag	gattggccatc	138240
atctcccatg	ggaagctgtg	ctgtgtgggc	tcctccctgt	ttctgaagaa	ccagctggga	138300
acagggtact	acctgacctt	ggtcaagaaa	gatgtggaat	cctccctcag	ttcctgcaga	138360
aacagtagta	gcactgtgtc	atacctgaaa	aaggtgagct	gcagtcttgg	tgctgggctg	138420
gtgttgggtc	tgggcagcca	ggacttgtct	gctgtgaatg	atttctccat	ctccaccctc	138480
tttgccatgt	tgaaccacc	atctccctgc	tctgttgccc	ctttgaaatc	atatcatact	138540
taaggcatgg	aaagctaagg	ggccctctgc	tcctattgtg	ctagttctgt	tgaatccgt	138600
tttcttttct	ctatgaggca	cagagagtga	tggagaaggt	ccttagagga	cattattatg	138660
tcaaagaaaa	gagacttgtc	aagaggtaa	agccttggtc	ancaaatgac	ctggtngttc	138720
ctgctcatta	cttttcaatc	tcattgacct	taacttttaa	actataaaac	agccaatatt	138780
tattaggcac	tgatttcatg	ccagagacac	tctgggcant	gaaagaaagt	aatgataata	138840
gttaatttta	tatagcgttg	ttaccattta	caaccttttt	ttttttttta	acctctatca	138900
tctcaattaa	agtgcagaga	gaccctggga	agaaggtaac	tatatattat	atcccagatg	138960
agggagagtga	ggcttgtagg	gaattggtag	ctgattcaag	gtcaccacgc	aggtaaataa	139020
cagtgggtgg	accagaccca	attaccaggt	atgttttctc	ctgtaccgca	gtacatgcct	139080
gagatttatt	tgtgtgttga	agccagtgg	acctaatgta	tttacctccc	aaactgaaac	139140
tcctatccac	ttatttacct	tttaatgagc	ctcttaactc	aagtgcagtc	tgaggaccag	139200
cagcatcagg	atcacttggg	aacttgttag	aaattcagca	acctgggccc	agctcagacc	139260
taccgaatca	gaactgtgtc	attttaacaa	ggttcttgag	tggttgaaca	cacattaaag	139320
catgagaagc	attgaactag	acatgtagcc	aggtaaaggc	cttgccctgag	atgggtggga	139380
aaggcctcat	tgacagcttc	attggcaggc	cacagttctt	tgggcagctc	tgcttccctga	139440
cctttcaccc	tcagggaagcg	aggctgttca	cacggcacac	acatgccaga	cagggtcctc	139500
tgaagccacg	gctgccagtg	catgtgtccc	agggaaagct	ttttccttta	gttctcacac	139560
aacagagctt	cttggaagcc	ctccccggcg	aaggtgctgg	tggtctctg	ttgctccgtc	139620
cctgaccctg	tctcacctcc	ttctttgcca	tcaggaggac	agtgtttctc	agagcagttc	139680
tgatgtggc	ctgggcagcg	accatgagag	tgacacgctg	accatcggtg	aggactctgg	139740
ggtttcttat	tcagggtggg	cctgagcttc	ccccagctgg	gcagagtggg	ggcagaggag	139800
gagaggtgca	gaggctgggtg	gcgctgactc	aaggtttgct	gctgggctgg	ggctgggtgg	139860
ctgcgggkgt	gggagcagct	tggtggcggg	ttggccta	gcttgcctgg	gtgcctgggg	139920
ctcggtttgg	gagctagcag	ggcagtgctc	cagagagctg	agatgattgg	ggtttggggg	139980
atcccttagg	ggagtggaca	ctgaatacca	gggatgagga	gctgagggcc	aagccaggag	140040
ggtgggattt	gagcttagta	cataagaaga	gtgagagccc	aggagatgag	gaacagcctt	140100
ccagattttt	cttgggtagc	gtgtgtagga	ggccagtgct	accagtagca	tatgtggaac	140160

agaagtcttg	acccttgcta	tctctgcta	gtcctaattg	ctggcttttc	ccaggaaggc	140220
ttctgcttcc	atggactgtt	agattaaccc	tttattttagg	taaatgaggg	aacctacttt	140280
ataagcatag	gaaaggggtga	agaatctttt	aagattccctt	tactcaagtt	ttcttttgaa	140340
gaatcccaga	gcttaggcaa	tagacaccag	actttgagcc	tcagttatcc	attcaccat	140400
ccaccacccc	acccacccat	ccttccatcc	tcccatcctc	ccattcacc	atccacccat	140460
ccagctgtcc	accatttcta	cactgagtac	ctataatgtg	cctggctttg	gtgatacaaa	140520
ggtgaataag	acatagtcct	ttcctttgcc	cccaacctc	agaccagaga	tgaacatgtg	140580
gaatgacct	aacacctgga	acaggtgtgg	tgtatgagcg	gcaggcctct	gatgagaggg	140640
tgggggagtg	ccagccctca	ctccgaagcc	cctctgagtt	gattgagcca	tctttgcatt	140700
ctgggtccctg	cagatgtctc	tgctatctcc	aacctcatca	ggaagcatgt	gtctgaagcc	140760
cggctggtgg	aagacatagg	gcatgagctg	acctatgtgc	tgccatatga	agctgctaag	140820
gagggagcct	ttgtggaact	ctttcatgag	attgatgacc	ggctctcaga	cctgggcatt	140880
tctagttatg	gcatctcaga	gacgaccctg	gaagaagtaa	gttaagtggc	tgactgtcgg	140940
aatatatagg	aaggccaaat	gtcctaaggc	cagaccagta	gcctgcattg	ggagcaggat	141000
tatcatggag	ttagtcattg	agtttttagg	tcatacgacat	ctgattaatg	ttggccccag	141060
tgagccattt	aagatggtag	tgggagatag	caggaaagaa	gtgttttcc	ctgtaccaca	141120
gtacatgcct	gagattttgtg	tggtgaaacc	agtgggtacct	aacacattta	catcccaacc	141180
ttaaactcct	atgcacttat	ttacccttta	atgagcctct	ttacttaagt	acagtgkgag	141240
gaacagcggc	atcaggatca	cttgggaact	tgtagaagaa	tcagcaactt	gggccccagt	141300
cagacctact	gaatcagaat	caggagcaat	tctctggtgt	gactgtgtca	cagccaggta	141360
tcaactggat	tctcatacat	aggaaatgac	aaacgtttat	ggatggatag	tctacttgtg	141420
ccaggtgctg	agattttgtt	tttgtttttt	gatttttttt	taatcactgt	gacctcattt	141480
aatttctcaa	aaaagatgaa	aaaatgaaca	ctcaggaatg	ctgacatgag	attcagaatc	141540
aggggtttgg	ggcttcaaag	tccatcctct	ctttatccat	gtaatgcctc	cccttagaga	141600
tacaacatca	cagaccttga	aggctgaagg	ggatataaaa	gctgtctggc	caagtgtgtc	141660
ccaagcttga	cagtgcagca	gaatcacctg	gggatattat	taaaaataaa	cataactaag	141720
tttggttcca	gggcctgtga	atcagaattt	ctggaggtga	ggccttgaag	tctgtatttc	141780
tattgcatac	tttgacaca	gtggtctata	gactagagtt	tggaaatgat	tgcgctcatt	141840
cagattctct	tctgatgtt	gaattgctgc	catcatattt	ctagtgtctc	atttctcct	141900
gctcattctg	tcttgataa	cttatcatag	tactagccta	ctcaaagatt	tagagccaca	141960
gtcctgaaag	aagccacttg	actcattccc	tgtaggttca	gaataaattt	cttctgcgca	142020
gtgtctgtca	tagctttttt	ttaaattttt	tttatttttg	atgagactgg	agttttgtct	142080
ttattgccc	agctggagtg	cagtgggtgc	attttggctc	actgcaacct	ccacctccca	142140
ggttcaagcg	atttctctgc	ctcagcctcc	caagtagctg	agattacaag	catgtgtctac	142200
cacgcccagc	taattttgta	tttttagtag	agatgggttt	tatccatgtt	ggtcaggctg	142260
gtctcgagct	ccagacctca	ggtgatctgc	cgcctcggc	ctcccaaagt	gctgggatta	142320
taggcctgag	ccacagcgct	cagccataac	tttaatttga	aaatgattgt	ctagcttgat	142380
agctctcacc	actgaggaaa	tggtctctgg	caaaaacggc	ttctctccca	ggtaactctg	142440
agaaagtgtt	attaagaaat	gtggcttcta	ctttctctgt	cttacggggc	taacatgcca	142500
ctcagtaata	taataatcgt	ggcagtggtg	actactctcg	taatgttgg	gcttataatg	142560
ttctcatctc	tctcattttc	cagatattcc	tcaaggtggc	cgaagagagt	ggggtggatg	142620
ctgagacctc	aggtaactgc	cttgaggag	aatggcacac	ttaagatagt	gccttctgct	142680
ggctttctca	gtgcacgagt	attgttctt	tccctttgaa	ttgttctatt	gcattctcat	142740
ttgtagagtg	taggtttgtt	gcagatgggg	aagggtttgt	ttgttgtaaa	taaaataaag	142800
tatgggattc	tttcttctgt	ccttcagatg	gtaccttgcc	agcaagacga	aacaggcggg	142860
ccttcgggga	caagcagagc	tgtcttcgcc	cgttcactga	agatgatgct	gctgatccaa	142920
atgattctga	catagaccca	ggctctgttag	ggcaagatca	aacagtgctc	tactgtttga	142980
atgtgaaatt	ctctctcatg	ctctcacctg	ttttcttttg	atggccttta	gccaagggtga	143040
tagatcccta	cagagtccaa	agagaagtga	ggaaatggta	aaagccactt	gttctttgca	143100
gcatcggtga	tgtgatcaaa	cctgaaagag	cctatccata	tcacttctct	taaagacata	143160
aagatgggtg	ctcaatcctc	tgaacccatg	tctttattat	cttttctgcg	gggtcctagt	143220
ttcttgata	cattaggtgt	ttaattgttg	aacaaatatt	cattcgagta	gatgagtgat	143280
tttgaaagag	tcagaaaggg	gaatttgctg	ttagagttaa	ttgtacccta	agacttagat	143340
atttgaggct	gggcatgggtg	gctcatgcca	gtaatcccag	cgctttgaga	ggctgagggtg	143400

ggtagatcac	ctgagggtcag	gagtttgaga	ccagtctgac	caacaagggtg	aaaccccgctc	143460
tctactaaat	acaaaaaatt	agccgagtg	gggtggcacat	gcctgtcatc	ccagctactt	143520
gggaggctga	ggcaggagaa	tcgcttgaa	ccaggaggca	gaggttgac	tcagccacgg	143580
ttgcgccatt	gcactccaga	ctgggcaaca	agagtgaata	ctccatctca	aaaaagaaaa	143640
aaaaagaatt	agatatattt	gatgagtg	tctttgtgtg	tttaactgag	atggagagga	143700
gagctaagac	atcaaacaaa	tattgttaag	atgtaaaagc	acatcagtta	ggatcatta	143760
gttttaggaca	aggatttcta	gaaaattttt	aggaacagaa	aactttccag	ttctctcacc	143820
cctgctcaaa	gagtgtatgg	ctcttacatt	atatataact	gcctgacttc	atacagtatc	143880
agtacttaga	tcatttgaaa	tgtgtccacg	ttttaccaaa	atataatagg	gtgagaagct	143940
gagatgctaa	ttgccattgt	gtattctcaa	atatgtcaag	ctacgtacat	ggcctgtttc	144000
atagagtagt	ctataagaaa	ttgatgactt	gattcatccg	aatggctggc	tgtaacacct	144060
ggttacgcat	gaacacctct	tttcagttgt	ctcaagacac	ctttcttttc	tgtacttata	144120
agacaaggac	tgaaggcag	agactgctac	tgttagacat	tttgagtcaa	gcttttcctt	144180
ggacatagct	ttgtcatgaa	agccctttac	ttctgagaaa	cttctagctt	cagacacatg	144240
ccttcaagat	agttgttgaa	gacaccagaa	gaaggagcat	ggcaatgccg	aaaacaccta	144300
agataatagg	tgaccttcag	tgttggcttc	ttgcagaatc	cagagagaca	gacttgctca	144360
gtgggatgga	tggcaagggg	tcctaccagg	tgaaggctg	gaaacttaca	cagcaacagt	144420
ttgtggccct	tttgtggaag	agactgctaa	ttgccagacg	gagtcggaaa	ggattttttg	144480
ctcaggtgag	acgtgctggt	ttcgccagag	actctggctt	catgggtggg	ctgcaggctc	144540
tgtgaccagt	gaaggcagga	tagcatcctg	gtcaagatat	ggatgccgga	gccagattta	144600
tctgtatttc	aatcccagtt	ctattccttg	ccagtttgtt	atccgctggc	aagtacttct	144660
tctatgcctc	aatctcctca	tctgtaaaat	ggggataata	atattacctg	caatacaggg	144720
ttgtttacgaa	aataaaaaatg	aataggtgct	tagaatgggg	cctgacatta	gtaaagtgtt	144780
agtttttgtgt	gtgtatatgt	tatttttatt	ttggaggaga	acataaaaag	gacaaagtgt	144840
agaaaaactg	gttgggtgta	ttcagctgtc	ataacatgag	agttgttatg	cccagatgca	144900
cttgacatgt	gaattttatta	gaaacatgat	ttttctctga	gttgatgttt	aactcaaact	144960
gatagaaaag	atagggtcaga	atatagttgg	ccaacagaga	agacttggtt	gactattgtc	145020
tgcattgtcag	tgtttgcacg	ctaacttgct	tagttagaaa	ggttaaaatt	tttactctta	145080
taaaatcaag	aaatatagag	aaaaggctctg	cagagagtct	ttcatttgat	gatgtggata	145140
ttgttaagag	cgggagtttg	gagcatacag	agctcaagtt	gaatcctgac	tttgcacttt	145200
attggctata	tgaccttggg	caagctgctt	agtctctctg	atcctcagtt	acctttgttt	145260
gttgatgatg	accattgata	acacaacct	aaataatgac	aacatagaga	tagttctcat	145320
tatagtagtt	gttatacaga	attattcact	caatgttaat	tttctgcatt	gaaatcccag	145380
aacattagaa	ttgggggcat	tatttgaatc	tttaagggtta	taaggaatac	atttctcagc	145440
aataaatgga	aggagttttg	ggttaactta	taaagtatac	ccaagtcatt	tttttttcag	145500
agaagatatg	gtagaaagtc	ttaggagggt	gaagaaggaa	ttggatattt	attctttctg	145560
agactatcat	gggagataat	gactatgggt	gtccatgatt	ggagccgttg	ctgtagagtt	145620
ggtttttatta	tagtgttaga	tttgaatggg	ccatgtgttc	tcagacctca	gattaaaawg	145680
agaaaaactga	ggccagtggg	gagcgtgact	tcacatgggt	acacttggtc	tagagacaga	145740
accaggattc	aggacttctg	gctcctggtc	ctgggttcat	ggcccaatgt	agtctttctc	145800
agtcttcagg	aggaggaagg	gcaggacca	gtgttctgag	tcacctgaa	tgtgagcact	145860
atttacttcg	tgaacttctt	ggcttagtgc	ctctgccagg	tggccataac	ctctggcctt	145920
gtgttgccag	agaaaaaggt	tagttttcag	gctccattgc	ttcccagctg	ccaagaatgc	145980
cttgggtgcag	cacagtcata	ggccctgcat	tcctcattgc	cgtgctgggt	ggtcggggag	146040
gtgggctgga	ctcgtaggga	tttgccccct	ggccttggtt	ctaacacttg	ccgtttcctg	146100
ctgtccccct	gccccctcca	ctgcctgggt	aaagattgtc	ttgccagctg	tgtttgtctg	146160
cattgccccct	gtgttcagcc	tgatcgtgcc	accctttggc	aagtacccca	gcctggaact	146220
tcagccctgg	atgtacaacg	aacagtacac	atttgtcagg	tatgtttgtc	ttctacatcc	146280
caggaggggg	taagattcga	gcagaccaaa	gatgtttacg	agggccaagg	gaatggactt	146340
cagaattaca	cgggtggaatg	aattttactg	ctgaggctca	ggccctgta	taagctaata	146400
ctgcatgcat	agaacagcag	cgaactaacc	ctgaataata	ggccagctct	ctgttgagcc	146460
tttcagcttc	tctctcttc	atcctactgt	tgtcaggaac	agccacatgt	gttttaggtg	146520
aaataatcca	cccttgcaaa	aatccatgat	taagttataa	aatatttgga	tttgtggagc	146580
tgtgttttaa	ttctgtaact	gagtcacagg	gcacactgtc	aaagcataga	acctccagag	146640

acttgttttc	tgcaaagtat	aattcatgta	attattatct	attctgttat	atttgggatg	146700
ttaggttagtg	tttgttcttt	agataaaaaat	atccccact	ctgtaacaat	acattaaatc	146760
aaagaaaagg	acaaaggatt	tttctgggtc	ttgttagcag	gagctttctt	cagtcctgaa	146820
agattttag	acctgtagat	gggggaactg	tgtagtgat	acaaaaggga	agcattttaa	146880
aaaaaaaaag	tatatatata	tatatatata	tatatatgta	atgtgaattg	gcctcttttt	146940
ctctaagncc	cacattttnc	ttcttacata	gttcagggtt	actttatttt	ttcctttccg	147000
gctgctgacc	ctgtattgoc	cgtagttgtg	gaacatagca	tgtgtttgtg	acctgtgcct	147060
gttatttttg	tgctttctag	ttgtgcatgc	aaagagtaca	aagttttctt	gccctttctt	147120
ggaaaatcct	gcttgtctgt	gccaaaggga	taattgtgaa	agcacttttg	aaatacttaa	147180
tgagttgatt	ttcttcaa	taaaaaaat	atataaatgt	atatgtgtat	gtacatgtgt	147240
gtacacatac	acacctttat	acatacagcc	cattttaa	aagctccact	ttggagtgtc	147300
ctacgtcacc	ctgatgccga	atacagggcc	agagtctgag	atccttctgg	gtgggttctg	147360
tggtttgttc	atcttctgtt	taagagcctg	tcacagagaa	atgcttctta	aaatgtttaa	147420
ttcttaaaaa	cttttttatc	tctcgattac	tggtttta	gaattactaa	gctggctgcc	147480
tctcatgtac	ccacagcaat	gatgtctctg	aggacacggg	aaccctggaa	ctcttaa	147540
ccctcaccaa	agaccctggc	ttcgggaccc	gctgtatgga	aggaaaccca	atcccgtgag	147600
tgccacttta	gccataagca	gggcttcttg	tgcttgttgc	ctggtttgat	ttctaata	147660
ctgcatttat	caactgcatg	ccacattgtg	accgccagca	tttgccctt	gaattattat	147720
tatgttttat	ttacaaaaag	cgaaggtagt	aaccgaacta	aattatctag	gaacaa	147780
ttggagagtc	ttctaacacc	gtgcaaagca	cgtcattaca	gacatttgtt	tactgattta	147840
gaaccttaat	atttaattta	aatangcact	ttacacttac	tgatgaaatg	cttttctctt	147900
ctttctctcc	cagcccctgt	acttaagtgc	ttcaataggc	tctcattata	tatgattttt	147960
aggttttgct	tatcagcttc	ttcgctttta	taacttgaaa	agatggcata	tgaattttta	148020
taaaaaggga	cactttcttc	ttctcaaat	gtatattttt	attgtacttt	ccttcaaa	148080
ccccttttta	aaagtaagca	gtggataaat	aaattcagtg	aagcatccat	atgaccctta	148140
agttagtgta	ggggaaggga	ggtcaccaga	tcactgtgag	tgaagatggt	ggagaggtga	148200
ggatcttatg	aggccgtgct	caaggctggg	agaggtgggt	tagtgtttcc	aggtttaggc	148260
agaatctcag	ctgaggctcat	gaaacaacag	tgatctctga	aaaattatgg	caagggtgga	148320
agggtgctgga	gaattggaga	gggggcaaac	ttgactttca	agtttcaatg	ggaagatagg	148380
tgactctgca	caccacagaa	cagttagcat	gataacctgt	ttatacaagg	ttctagagca	148440
gatttctaaa	tggatagcta	ctgtgtgctt	gtttgttctt	aattagtatt	ggatagttac	148500
taataacttg	ttagtactta	gtacataatg	ggtggtaaat	cctagcagct	aatattggtt	148560
cccaataaac	cagatgacaa	ggatagagaa	ggacacagac	acggcctatc	tggattttcat	148620
gggtgcctttg	atcttccaca	tgaagggtgt	gtagggaaga	tagaagcatg	agatgagatg	148680
ataatatagt	tatctggatt	catcactggc	cagctgaacc	atatgaactc	atggattgat	148740
gctagcttag	gaaggctctg	taggagccag	aactgggctg	agagccagcc	catagagaca	148800
aaagaggccc	ggccctgaca	tcagagggtt	caaacatgat	gtctgagccc	cacctacagt	148860
ctgccggagg	tggttggaag	gaagagcctt	tatccttaca	attccttactg	aaattcaaat	148920
tttttaggttt	tgcaaaaaaa	tggtggacct	gaaggaaatt	tgacaggagc	atgtctcagc	148980
tgtattttaa	tttgtctcag	ccaatccccct	tttgaatgtt	cagagtgtaa	gcttcaggag	149040
ggcagcgcgt	cttagtgtga	cttttctggg	cagttcaggt	gctttaagga	gacaattaga	149100
gatcaatctg	gaaaacttca	tttgaatttt	taatacataa	gaaaacaata	agaaatagtt	149160
aaaaatatat	atattatata	tatatatgtg	tgtgtgtgtg	tgtgtgtgtg	tatatatata	149220
tatatnttta	tttnatttat	ttnnnnnnnn	ttttttgaga	tggagtctcg	ctctgttgcc	149280
caggctggag	tgcagtggct	caatcttggc	tcactgccac	ctctgcctcc	caggttcaag	149340
tgattctcct	acctcagcct	cctgagtagc	tgggattaca	agcatgtgcc	accacactgg	149400
ctaatttttc	taatttttagt	agagatggag	tttcaccatg	ttggacagga	tggtcttgaa	149460
ctcctgactt	agtgatccac	ccgccttcgc	ctcccaaagt	tctgggatta	caggcatgag	149520
ccatcgtgcc	tggcaattat	atttaatat	taataataag	gaaataattg	ctgtaacttt	149580
actttaaatt	gtggaattct	gaaactggaa	gggaactgga	aatgacttgt	tgaatcaaat	149640
catttttaaac	ttttattttg	ccagtggaaa	aaataagccc	ccaaaagagc	aggggacctg	149700
ctgna'tgtcc	cacagtaatt	cagagctgga	gatgaggttg	aaggctttgt	gtcttatctc	149760
cagggaaaat	ttgtagacag	cgtagctctn	ttatgtgacg	agcattctca	cccagtcatt	149820
cccccaattc	tctactcatt	tgagaacata	aattggatct	tgccagtcct	tactcatttt	149880

tcagcacatc	gagcataaga	tccagactct	ttcccaggcc	tctctcatct	ggctcctctc	149940
ctcctccttt	atcattactc	ttcttcgtag	cttatcctac	tccagccatg	ctgtcttctc	150000
attattccta	aaaartagaa	atgcattttc	tcctagggcc	tttgtacctg	cacttgccat	150060
cgcttttgct	cagaatgttc	tttttgccaa	gcttttgccc	agcttggtct	ccatcattgt	150120
tatgttttgg	ctgaaatgtc	ttctcttagt	aggttcattc	tccccagtca	ctgtcttttt	150180
attttgcttt	attttgggcc	atctaagggt	atcttattag	tgtatttgtt	gttcgtctcc	150240
tccatgggca	tacacctcca	tgaaggcagg	tatttttcacc	ttagggccctc	gaatatactg	150300
gacagcatct	ggcacgtagt	agatgtctaa	cgaatgtttg	ttgtgtgagc	aaatggttgg	150360
ttgattggat	tgaactgagt	tcagtatgta	aatatttagg	gcctctttgc	attctatttt	150420
acttatgtat	aaaatgatac	ataatgatga	tataaatgat	gtcacagtgt	acaaggctgt	150480
tgtgggatca	agcaatcaaa	tgagatcatg	cttgtctttt	ccaaatgggt	aggggaataga	150540
tgcattgtttg	tgggtgtttac	ggaatgatcc	tgtgtctctg	aggcaacaga	aaggccaggc	150600
catctctggg	aatcctactc	ttgtgtgtct	ccctttgcag	agacacgccc	tgccaggcag	150660
gggaggaaga	gtggaccact	gccccagttc	cccagaccat	catggacctc	ttccagaatg	150720
ggaaactggac	aatgcagaac	ccttcacctg	catgccagt	tagcagcgac	aaaatcaaga	150780
agatgtctgcc	tgtgtgtccc	ccaggggag	gggggctgcc	tcctccacaa	gtgagtcact	150840
ttcagggggt	gattgggcag	aaaggggtgca	ggatgggctg	gtagcttccg	cttggaagca	150900
ggaatgagt	agatatcatg	ttgggaggg	ctgtttcagt	cttttttgtt	ttttgttttt	150960
ttttctgagg	cggagtcttg	ctctggctgc	ccaggctgga	gtgctgtggc	atgatcttgc	151020
ctcactgcaa	cctccacctc	ccagggtcaa	gcgattctcc	tgcctcagcc	tcctgagtag	151080
ctgggattac	aggcacgcac	caccatgtct	ggctaatttt	tgtgttttta	gtagagatag	151140
ggtttctgccc	tgttggctag	gctggctctg	aattcctgac	ctcaggtgat	ccacccgcct	151200
cgccctccca	aagtgtctgg	attacaggcg	tgagccacta	cgccagccc	tgtttcagtc	151260
tttaactcgc	ttcttgcctc	aagaaaaagc	atgtgagttt	tgaggggaga	aggtttggac	151320
cacactgtgc	ccatgcctgt	cccacagcag	taaagtcaca	ggacagactg	tggcaggcct	151380
ggcttccaat	cttggctctg	caacaaatga	gctggttagc	tttgacaggc	ctgggcctgt	151440
ttcttcacct	ctgaattagg	gaggtctggc	cagaaaaactc	ctgtggatct	tgtcaactct	151500
ggtattctta	gagactctgt	ttgggaagga	gtcctgagcc	attttttttt	tcctgagaat	151560
ttcaggaaga	ggagtgttta	tgtagctctc	ctgctgcttt	tatcagcaac	caaattgcag	151620
gatgaggaca	agcaattcta	aatgagtaca	ggaactaaaa	gaaggcttgg	ttaccactct	151680
tgaaaataat	agctagtcca	ggtgcgggg	ggctcacacc	tgtaatctca	gtattttggg	151740
atgccgaggt	ggactgatca	cctaagggtca	ggagttcgaa	accagcttgg	ccaatgtggc	151800
gaaaccctgt	ctctactaaa	aattcaaaaa	ttagccaggc	atggtggcac	atgcctgtaa	151860
tcccagttac	ttgggaggct	gaagcaggag	aattgcttga	acctgggagg	tggaggctgc	151920
agggagccaa	aattgcgcca	ctgtactcca	gcctgagcaa	cacagcaaaa	ctccatatca	151980
aaaaataaaa	tgaataaaat	aacagcta	ctagtcatca	gtataactcc	agtgaacaga	152040
agatttatta	ggcatagtga	atgatgggtc	ttcctaaaaa	tctcttgact	acaaagaatc	152100
tcatttcaat	gtttattgtt	tagatgttca	gaataaatcc	ttgggaaaga	ccttggcttg	152160
gtgtaagtga	attaccagt	ccgagggcag	ggtgaaccaa	gtctcagtgc	tgggtgactg	152220
agggcagtg	ctgggacctg	tagtcagggt	tcgggtcaca	ctgtggacat	ggtcactgtt	152280
gtccttgatt	tgttttctgt	ttcaattctt	gtctataaag	acctgtatgc	ttggttttca	152340
tgtgatgaca	gagaaaacaa	aacactgcag	atatccttca	ggacctgaca	ggaagaaaca	152400
tttcggatta	tctgggtgaag	acgtatgtgc	agatcatagc	caaaagggtga	ctttttacta	152460
aacttggccc	ctgcocktatt	attactaatt	agaggaatta	aagacctaca	aataacagac	152520
tgaacacagt	ggggaaatgc	cagattatgg	cctgattctg	tctattggaa	gtttaggata	152580
ttatcccaaa	ctagaaaaga	tgacgagagg	gactgtgaac	attcagttgt	cagcttcaag	152640
gctgaggcag	cctgggtctag	aatgaaaata	gaaatggatt	caacgtcaaa	ttttgccact	152700
tagtagcaac	ttgaccagg	aactggttat	ccttttaaa	ccttagttta	tctaaattgt	152760
gatattaatg	ttgctcttat	aagtttgtca	tgaggactaa	attaaatggt	gtacatagag	152820
tgccttgggt	actctctgat	gggggactcc	atgataat	gtggtctcat	ggagggagct	152880
ctgggaaggt	ttaggagcct	gccttggctc	tgcagccttg	ggagagcctt	ctagcttccc	152940
aggacatggc	agcclagtgt	tgaatgcttg	gctcagcaaa	tgtttgtctc	cgtttctctc	153000
ccatcaactt	ggtcagttgg	ggtcttccag	ttaggagtat	ctcagtgact	ttaaatggca	153060
tgggcatgct	ggagtgatag	tgaccatgag	tttctaagaa	agaagcataa	tttctccata	153120

tgatcatccac	aattgaaata	ttattgttaa	ttgaaaaagc	ttctaggcca	ggcacggtgg	153180
ctcatgcctg	taatcccagc	acttttaggag	gccaaaggcg	gtggatcact	tgaggtcagg	153240
agtttgagac	cagcctggcc	aacatgggga	aaccctgtct	ctactaaaaa	tacaaaataa	153300
gctgggctg	gtggtgctg	cctgtaatcc	cagctacttg	ggaggctgag	gcaggagaat	153360
tgcttgaatc	tgggaggcgg	aggttgaggt	gagctgagtt	catgccattg	cattccagcc	153420
tgggcaacaa	gagcgaaacc	atctcccaaa	agaaaaaaa	aagaaagaaa	aagcttctag	153480
tttgggtaca	tcttgggtcta	taaggtgggt	tgtaaattgg	tttaacccaa	ggcctgggtc	153540
tcatataagt	aatagggtat	ttatgatgga	gagaaggctg	gaagaggcct	gaacacaggc	153600
ttctttttct	tagcacaacc	ctacaaggcc	agctgattct	agggttattt	ctgtccgttc	153660
cttatatcct	caggtggata	tttactcctt	ttgcatcatt	aggaataggc	tcagtgcttt	153720
ctttgaactg	atTTTTgtt	tctttgtctc	tgcagcttaa	agaacaagat	ctgggtgaat	153780
gagtttaggt	aagttgctgt	ctttctggca	cgtttagctc	agggggagga	tggtgtgtga	153840
ggtgtncctg	gattgaaaga	agccttgggg	attgtttgtc	actcacacac	ttgtgggtgc	153900
catctcactg	tgaggaggac	agaagccctg	tgaacatgtg	gagcacacag	gggcacagac	153960
agatttagat	taggcctgct	ttatagagtt	tctgcctaga	gcatcatggc	tcagtgccca	154020
gcagccctc	cagaggcctc	tgaaatattt	gatatactga	tttctctgag	gagaatcaga	154080
aatctcctgc	aggtgtctag	ggatttcaag	taagtagtgt	tgtgagggga	atacctactt	154140
gtactttccc	cccaaacccag	attccccagg	cttcttaagg	actcaaggac	aatttctagg	154200
catttagcac	gggactaaaa	aggtcttaga	ggaaataaga	agcgccaaaa	ccactctttt	154260
gcactgtatt	tcaacccatt	tgtccttctg	ggttttgaag	gaacagggtg	gactggggac	154320
agaagagttc	ttgaagccag	tttgtccatc	atggaaaatg	agataggtga	tgtggctacg	154380
tcagggggcc	cgaaggctcc	ttgttactga	tttccgtctt	ttctctctgc	cttttcccca	154440
agggccagga	cccctggatc	tctgggcaga	gcagacgcag	gcccctataa	tagccctcat	154500
gctagaargg	agccggagcc	tgtgtataag	gccagcgcag	cctactctgg	acagtgacag	154560
gttcccactc	tcccactcc	ccatctgctt	gcctccagac	ccacattcac	acmcgagcca	154620
ctgggttggg	ggagcatctg	tgagatgaaa	caccattctt	tcctcaatgt	ctcagctatc	154680
taactgtgtg	tgtaatcagg	ccaggctcct	cctgctgggc	agaaaccatg	ggagttaaga	154740
gattgccaac	atatttaga	ggaagctgac	gtgtaacttc	tnngaggcaa	aatttagccc	154800
tcctttgaac	aggaatttga	ctcagtgaac	cttgtacaca	ctcgactga	gtctgctgct	154860
gatgatactg	tgcacccccc	tgtctgggtt	ttaatgtcag	gctgttcttt	taggtatggc	154920
ggcttttccc	tgggtgtcag	taatactcaa	gcacttcctc	cgagtcaaga	agttaatgat	154980
gccatcaaac	aaatgaagaa	acacctaag	ctggccaagg	taaaatatct	atcgttaagt	155040
gtatcagaaa	aatgggcatg	tagctgctgg	gatataggag	tagttggcag	gttaaacgga	155100
tcacttgcca	ctcattgttt	ctgaatatgt	tggtacacag	agccgtcttt	ggcatttagc	155160
gatttgagcc	agacaaaact	gaattactta	gttgtacgtt	taaaagtgtg	ggtcaaaaac	155220
aaatccagag	gccaggagct	gtggctcatg	cctgtaatcc	tagcactttg	ggaggctgaa	155280
gcgggtggat	cacttgaggt	caggagttcg	agaccagcct	ggcctacatg	acaaaacccc	155340
gtatctacta	aaaatacaaa	aaaattagct	gggctttggtg	gcacacacct	gtaatcccag	155400
ctacttggga	ggctgaggca	ggagaattgc	ttgaaccctg	taggaagagg	ttgtagttag	155460
ccaagatcgc	accgttgcac	tccagcctgg	gcaacaagag	caaaactcca	tctcaaaaaa	155520
caaattaaat	ccagagattt	aaaagctctc	agaggctggg	cgcggtgggt	tacacctgtt	155580
atcccagcat	tttgggatgc	cgaggcgggc	aaagcacaa	gtcaggaggt	tgagaccagc	155640
ctggccaaca	tagtgaaacc	ctgtctctgc	taaaaacata	gaaaaattag	ccgggcatgg	155700
tggcgtgctg	ctgtaatccc	agctactcgg	gaggctgagg	tgagagaatt	rcttgaaccc	155760
gggaggcgga	ggttgcagtg	agcccagatt	gcaccactgc	actccagcct	gggcgacaga	155820
gcaagactcc	atctcaaaaa	aagctctcag	aacaaccagg	tttacaattt	tggtcagttg	155880
gtaaataaac	tgggtttcaa	acatactttg	ctgaaayaat	cactgactaa	ataggaaatg	155940
aatctttttt	tttttttttt	taagctggca	agctggctctg	taggacctga	taagtaactca	156000
cttcatttct	ctgtgtctca	ggtttcccat	tttttaggtga	gaattaaggg	gctctgataa	156060
aacagaccct	aggattgtgg	acagcagtgr	tagtcctaga	gtccacaagt	ctgcttttga	156120
gtgatggggc	catgtatctg	gcacatctgc	aggcagagcg	tggttctggc	tcttcagatg	156180
atgccggtgg	agcactttga	ggagtctcca	ccccaccgtg	ataaccagac	attaaaaatct	156240
tggggctttg	catcccagga	tttctctgtg	attccttcta	gacttgtggc	atcatggcag	156300
catcactgct	gtagatttct	agtcacttgg	ttctcaggag	ccgtttattt	aatggcttca	156360

catttaattt	cagtgaacaa	ggtagtggca	ttgtctttca	cagggccgctc	ctgtttgtcca	156420
caggttccag	attgactgtt	gcccccttatc	tatgtgaaca	gtcacaaactg	aggcaggttt	156480
ctgtttgttta	caggacagtt	ctgcagatcg	atttctcaac	agcttgggaa	gatttatgac	156540
aggactggac	accaraaata	atgtcaaggt	aaaccgctgt	ctttgttcta	gtagcttttt	156600
gatgaacaat	aatccttatg	tttctctggag	tactttcaac	tcatggtaaa	gttggcaggg	156660
gcattcacaa	cagaaaagag	caaaactatta	actttaccag	tgaggcagta	cgggtgtagt	156720
tagtgattca	gagaatttgc	tttgccacca	gacataccag	gtaaccctga	ctaagttact	156780
taacctatct	aaacctcagt	tycctcatct	gtgaaatgga	gacagtaatc	atagctatct	156840
ccaaactggt	gtgagaattc	aatgagttaa	aggataaagg	tcctcaccac	agcgccctgcc	156900
cacatagtca	gtgatcacta	tgctctgaac	actgtaatta	cttcgccata	ttctctgac	156960
atagtgtttt	gccttggtat	gtgactagaa	tttctttctg	aggtttatgg	gcatggttgg	157020
tgggtatgca	cctgcctgca	ggagcccggt	ttgggggcat	tacctgttac	ctgggtatgt	157080
ttctttcagg	tgtggttcaa	taacaagggc	tggcatgcaa	tcagctcttt	cctgaatgtc	157140
atcaacaatg	ccattctccg	ggccaacctg	caaaagggag	agaaccctag	ccattatgga	157200
attactgctt	tcaatcatcc	cctgaatctc	accaagcagc	agctctcaga	ggtggctctg	157260
taagtgtggc	tgtgtctgta	tagatggagt	ggggcaaggg	agaggggtat	ggagaagggg	157320
agaaaaatgt	gaatctcatt	gtaggggaac	agctgcagag	accgttatat	tatgataaat	157380
ctggattgat	ccaggctctg	ggcagaagtg	ataagtttac	gaattggctg	gttgggcttc	157440
ttgaactgca	gaagagaaaa	tgacactgat	atgtaaaaat	cgtaacattt	agtgaattca	157500
tataaagtga	agttcaaaaat	tgtaatttaa	attataattt	aattataagt	gtttaatcag	157560
tttgatttgt	ttaaaaacca	ctgtttttaa	tttgggtggaa	tatgttttta	ttagcttgta	157620
tctttaattc	ctaaatttaag	ctgtgtgtgt	gtgtgtgtgt	gtgtgtgtgt	gtgtgtgtgt	157680
gtgtgtgnnt	gtgaagttta	aagccaggat	gagctagttt	aaagtatgca	gcctttggag	157740
tcatacagat	ctggggttga	atctgggtct	taaactttat	agatgtatga	tattaaatga	157800
ggcagttcat	gtaaaattgcc	aagcccagca	ctcagcacag	agttgatatt	tcacacacat	157860
tagatacctt	tcctgtatgt	ggagcatggc	agttcctgtt	tctgctttac	tcctacagga	157920
tactaatata	ggacactagg	atctttatac	caagacccca	tgtaatgggc	ttatgagacc	157980
attcttctta	taaaaatctg	acagaatttt	tgatatgtgt	agatcaatag	gctgcatact	158040
gttattttca	agttgattta	cagccagaaa	tattaattta	tttgagtagt	tacagagtaa	158100
tattttctgct	ctcatttagt	tttcaagccc	cactagtcct	ttgtgtgtga	aaattttacaa	158160
cttactgctc	ttacaaggtc	atgaacagtg	gaccaaagtg	aatgccatta	accactctga	158220
cttctctcat	tagttttatt	gtgacagtgg	actcttttga	cctcagtaat	accagtttgg	158280
catttacatt	gtcatatttt	tagacttaaa	aatgatcctc	ttaaccctga	ataaaatgtg	158340
tctggtgaac	agatgttttt	ccttgggctg	tgccctcagat	atctctgtgt	gtgtgtacgt	158400
gtgtgtttgt	ctgtgtgtcc	atgtcctcac	tgattgagcc	ctaactgcat	caaagacccc	158460
tcagattttc	acacgctttt	tctctccagg	atgaccacat	cagtggatgt	ccttgtgtcc	158520
atctgtgtca	tctttgcaat	gtccttcctc	ccagccagct	ttgttgtatt	cctgatccag	158580
gagcgggtca	gcaaagcaaa	acacctgcag	ttcatcagtg	gagtgaagcc	tgctcatctac	158640
tggtctctca	attttgtctg	ggatatggta	aggacacagg	cctgctgtat	ctttctgatg	158700
tctgtcaggg	ccatggattg	atatggataa	gaaagaaaga	gctctggcta	tcatacaggaa	158760
atgttccagc	tactctaag	atgtatgaaa	aagaaatagc	cagaggcagg	tgatcacttt	158820
catgacacca	aacacagcat	tgggtaccag	agttcatgtc	acaccagagg	gaaaattctg	158880
tacacaaatga	tgaaaattaa	taccactacc	acttaagttc	ctatgtgaca	actttcccaa	158940
gaatcagaga	gatacaagtc	aaaactccaa	gtcaatgcct	ctaacttctc	tgatgggttt	159000
taacctccag	agtcagaatg	ttctttgcct	tactaggaaa	gccatctgtc	atttngaaaa	159060
ctctgtacat	tttatcagca	gcttatccat	ccattgcaaa	tantgttttt	gtgccagcca	159120
caatatattg	cttctatttg	gaccaatatg	ggggatttga	aggaattctg	aagttctaat	159180
tatatattcaa	ctctacttta	caatatctcc	ctgaaatata	tctccctgta	acttctatta	159240
attataagct	acacagagca	aatctaattc	ttctcccacc	gaacaagtcc	ctggatattt	159300
aaaaataact	ctcatactct	catttaacct	gagtattacc	cagataagat	gatatatgag	159360
aatacacctt	gtaacctccg	aagcactgta	caaagtgtgag	caatgatggg	ggagatgatg	159420
atgagatctt	tgtgttttat	accaagcccc	ttagactgtg	tcactcttct	gatccggttg	159480
tccttgtatg	gccatgctgt	atattgtgaa	tgtcccgttt	tcaaaagcaa	agccaagaat	159540
taaccttgtg	ttcaggctgt	ggtctgaatg	gttatgggtc	cagagggagt	tgatctttag	159600

ctcacacttc	tattactgca	gcacaaagat	tttgcathtt	ggaaggagca	ccgtcttact	159660
ggcaacttag	tggttaaacca	aaacctccat	ttcacacaaa	tgattgtgaa	attcgggtct	159720
ccttcattct	atacaaatct	atcttgatttt	tttgaaacta	aacttttat	ttatccat	159780
taaattacat	gggttttatt	tttgttttat	cttgattcag	taattactcc	tttcagtaaa	159840
cacagactga	gtgctgtgtg	tctgacttat	gccaggcata	ggtgattcag	agatgaaagg	159900
tcaagtccct	gaacccatct	cttgctcttc	gggtattat	ctgtccctcc	ctgctttaga	159960
gctcctgaaa	tttgctagaa	gcatgtcttc	atctaagttg	ttgataaaca	catcaagtag	160020
gattggactg	aggcagagcc	ctgtagtctg	aagctgcagt	tcttctagcg	gctgacaagc	160080
cccactatca	cttccctgct	ggtgctttgc	tctgccagct	gtgaattctc	ataattgtcc	160140
tatcgtaag	tctttatttc	tgcattttac	tgcttgatac	actgtcagga	cagactttaa	160200
aattattctc	agtgcgatga	aacaattctg	acattcatgt	tatgagcagt	tacctcataa	160260
atagattaca	tgtgagattg	aacttgggca	gactataata	tagcattaat	gatgaaacag	160320
acacagtcac	cttcgggaag	aagaatagag	gcttatttgc	tgctgtgaa	attaaaaatta	160380
ctctgactgg	gaatccatcg	ttcagtaagt	ttactgagt	tgacaccttg	gcttgactga	160440
tggaagaca	gaaaggcat	gtagtttata	aaatcagcca	aggggaaaat	gcttgctaaa	160500
atgtattgtc	gggtattttg	attaatagtt	tatgtggctt	cattaattca	gagttactct	160560
ccaatatgtt	tatctgccct	ttcttgtctg	ataatgggtg	aaacttgtgt	gatgcattgt	160620
atatttgatt	taggggtgaa	ctggatgtct	ttgttttcac	ttttagtga	attacgttgt	160680
ccctgccaca	ctggtcatta	tcattcttc	ctgtctccag	cagaagtcc	atgtgtccct	160740
caccaatctg	cctgtgctag	cccttctact	ttgtctgtat	gggtaagtca	cctctgagt	160800
agggagctgc	acagtggata	aggcatttgg	tgcccagtg	cagaaggagg	gcagggactc	160860
tcagtagaca	cttatctttt	tgtgtctcaa	caggtgggtc	atcacacctc	tcattgtacc	160920
agcctccttt	gtgttcaaga	tccccagcac	agcctatgtg	gtgctcacca	gcgtgaacct	160980
cttcattggc	attaatggca	gcgtggccac	ctttgtgctg	gagctgttca	ccgacaatgt	161040
gagtcattga	gagagaacac	tcctgctggg	atgagcatct	ctgggagcca	gaggacagt	161100
tttaattgtg	atcttattcc	acttgtcagt	ggtattgaca	ctgctgactg	ccttgtcctg	161160
tcttcagagt	ctgtcttccc	tgagaaggca	aagcaccttt	ctttcttgct	gtgccttaca	161220
ttttgctggt	caagcctttc	agtttctttt	gacagttttt	tttacttctt	tctttttcca	161280
atgttgctct	taccaagagt	agctcctctg	ccttccactt	tacacatgag	agctgggcga	161340
cgncattcag	tcctaaggct	tttaccatca	cctctcttgg	tgtttttatt	gtcatctcta	161400
agatcaatgc	ctttagcctt	gatcataacc	ttgaactcta	atctcaaatt	ctcacttgcc	161460
tagtggattg	ctccatttag	atagtatata	gataccccaa	cctggatatg	tcctagtttt	161520
ctttcccctt	ggaacttaat	gcttttcttg	ccatccctgt	cacactcagt	ggcactacca	161580
tccactcggt	tgcccaagct	ggctcttaga	gttatccctag	atgcttgctt	tgctgttgca	161640
gatttcccac	attcaactgg	ttatgtgtgc	agttcttcca	ggtatggacc	tctaaaataa	161700
ggcttccctc	ccattccggt	tgctattgcc	tttgtccaaa	cacagcacac	aaggcctttt	161760
acagttgcac	aactcttcc	gtccataccc	accacacctt	ttcccagctg	taagcttcag	161820
atgagttgcc	tccaaccacc	atgctcctgt	aggcctggct	tgaaatgccc	ttcttctgtc	161880
acaggtctg	gtagtatctc	ccttgccctt	caagatttag	ctaaaatgtg	aagctttcct	161940
tacctgctgg	gaggtgttct	ctcttttctc	tgtgctctca	gagtccttag	tccatgcctc	162000
cagtacaacg	tacatccact	tacatggtaa	tttctgtttt	acatactttt	cctactcgga	162060
gtggagtctg	tttcttaata	atcttgccct	tcccactgccc	tagcacagt	catccagcgt	162120
atagccctct	attcagttgg	tagatatttg	gccactgttg	ccttggtgga	tcataagttc	162180
tgatgtattt	gagaagaatt	tctaaaattc	tgacaaaatc	ctgaaactca	aatattgacc	162240
cagacatgag	caatttgctt	ttcaaagtct	aagggtattt	taatggattt	gctttaatta	162300
aatctagcct	gtttctaaag	tttattcatt	atttctccat	actcagagca	tttctccaga	162360
ttttctaaag	aatagaattt	tattgctaca	tatcatcagc	tatgcctgct	gctatttaatt	162420
tggtatctga	attaaaaggt	ctggtttgtc	cctagagaa	caaatttttt	cttactccc	162480
atatttcaga	acttgataca	tttttaggat	aaacctgaa	tgacaccctg	ttcttctccc	162540
tcacctccc	ttccctccca	tttttttttt	tttttttttt	tagaagctga	ataatatcaa	162600
tgatatcctg	aagtcctgtg	tcttgatctt	cccacatttt	tgctgggac	gagggctcat	162660
cgacatgggt	aaaaaccagg	caatggctga	tgccctggaa	aggtttgggtg	agtgaagcag	162720
tggtctgagg	atgctttaat	ggagatggca	ctctgcatag	gccttggtac	cctgaacttt	162780
gttttgaaa	gaagcaggtg	actaagcaca	ggatgttccc	ccaccccat	gcccagtgac	162840

agggtcatg	ccaacacagc	tggttggtggc	atgggtttttg	tgacacaacc	atgtgtctgt	162900
gtctctgata	gcattgagaa	aagtgaagg	gcagtttttga	aggtaaggaa	aatagtgtta	162960
tttgcttggg	tccactggct	catgccactg	tctgggttgg	ttagaagcac	tggaaaagtc	163020
aaaccataac	tttgagaatt	agggtgatcag	ggaatcagaa	ggaaagatgc	aaactttggc	163080
tcttttaggc	gaatcatgtg	cctgcagatg	aggctattta	ttatctttta	cacagtctat	163140
aaaattataa	tgtattacat	ctttttctac	ctttagaatg	gttaaaaaata	tttctccggt	163200
agccatata	ttattattca	tccattagat	aatatagtc	aatgggcat	gttattttact	163260
gttcatagaa	gaggggcttt	ttgcaacttg	ggctacaaag	gagatatgta	aggaatttaa	163320
ggaatgggta	catggaacta	gatttaattg	aatctagtgg	tttaattgat	tcactaggat	163380
atatgctact	gaaaggggaa	tctgcttaaa	gtgctttctg	atattttatta	ttactaaaaac	163440
ttagaattta	ttaaaaatac	tgactgtgaa	aattacttgg	gtcgtttgcc	tttttaaaag	163500
gatttttggc	atgtctcatt	aaaaaaagaa	atactagata	tcttcagtga	agttacaaat	163560
cgaatacaca	ttggctctga	aattctgatt	gatactgggt	cataaaaagt	tttcccaaat	163620
cagacttgga	aagtgatcac	tctcttgta	ctcttttttc	ctgtcatgg	gtgataagcca	163680
tttggttga	ttggaagatc	ggtgaatttt	aaggaacata	ggcccaaat	tgaggaaggg	163740
ccatgggttt	tgatccctcc	attctgaccg	gatctctgca	ttgtgtctac	taggggagaa	163800
tcgctttgtg	tcaccattat	cttgggactt	ggtgggacga	aacctcttcg	ccatggccgt	163860
ggaaggggtg	gtgttcttcc	tcattactgt	tctgatccag	tacagattct	tcacagggcc	163920
caggtgagct	ttttcttaga	acccgtggag	cactgtgttg	agggtcacag	aggaggcgca	163980
cagggaaaca	ctcaccaatg	gggttgcat	tgaactgaac	tcaaaatag	tgataaaact	164040
gattttctctg	atgtgggcat	cccgcagccc	cctccctgcc	catcctggag	actgtggcaa	164100
gtaggtttta	taatactacg	ttagagactg	aatctttgtc	ctgaaaaata	gtttgaaagg	164160
ttcatttttc	ttgttttttc	ccccagacc	tgtaaatgca	aagctatctc	ctctgaatga	164220
tgaagatgaa	gatgtgaggc	gggaaagaca	gagaattctt	gatgggtggg	gccagaatga	164280
catcttagaa	atcaaggagt	tgacgaaggt	gagagagtac	aggttacaat	agctcatctt	164340
cagttttttt	cagcttttatg	tgctgtaacc	cagcagtttg	ctgacttgct	taataaaagg	164400
gcagtgtgtc	ccaaaatgta	catctatacc	aaggttctgt	caattttatt	ttaaaaacac	164460
catggagact	tcttaaagaa	ttcttactga	gaattctttt	gtgatatgaa	ttcccatctt	164520
cgaatacatt	gggttttatat	gcttacattt	atgtgttagt	tattaaaaaca	tactaatatt	164580
gtatatctag	tcaaaactga	ggtagagaga	ataaatgggt	gattttgagt	ttgagtttca	164640
tagtccaaaa	agctgatata	ttgcctgtgt	tcaagagggt	ctatatcagc	cctctagatg	164700
ccagcatctc	caaattttac	ttttttggaa	tctgtacagt	atttgcaata	tttttattac	164760
aaatttctac	tctgtggaat	ttaattttta	aaatacctgc	aatacatata	tatgttgaat	164820
agatgaaaaa	ttatgtagat	rataatgaat	gatacgggtc	taaaaagaca	ggttaaaaag	164880
taagttcact	tttattttga	gcttcagaat	cattcagaag	ccagtcgcca	caaacgcaga	164940
ccaaggctct	tggcacatca	aatatgccta	tggcttaggg	ttattgacaa	gtcttatgtt	165000
gcagtgtatg	tggtttatag	tcctgccttc	cacagttgct	tgggagagct	gtgagtcact	165060
gaggcttatg	aatgtttaca	ttttgtttgt	tgcatagata	tagaagggaag	cgggaagcctg	165120
ctgttgacag	gatttgcgtg	ggcattcttc	ctggtgaggt	aaagacactt	tgtctatatt	165180
gcgtttgtcc	ctattagttc	agactatctc	tacccaatca	agcaacgatg	ctcgttaaga	165240
ggtaaaagtg	gatttttaaag	gcttctgtat	ttatgccagg	atggagcaat	tagtcatcga	165300
gaagagaggg	accctgtatg	tcaagagaat	gatttcagag	aatccaatac	aatttaagaa	165360
aaagcatggg	gctgggcgca	gtgattcact	cctgtaatcc	cagcactttg	ggaggccgag	165420
gtgggcgag	tcacgaggtc	aggagattga	gaccatctctg	gccaacatgg	tgaaacccca	165480
tctctactat	aaatacaaaa	attagctggg	catagtagtg	cattctctgta	gtcccagcta	165540
ctcgggaggg	tgaggcagga	gaattgcttg	aacctaggag	ggggagggtg	cccagattgc	165600
gctgctgcac	tcagcctgg	tgacagagtg	agactcatgt	caacaacaaa	aacagaaaaa	165660
gcacgcacat	ctaaaacatg	cttttgtgat	ccatttgggg	tggtgatgac	attcaaatag	165720
ttttttaaaa	atagattttc	tcctttctgg	tttccgtttg	tgttctttta	tgcccttttg	165780
ccagagtagg	tggtgcnaat	ttggctangc	tggttttcat	tactgttttt	cacnacnatt	165840
aacntttggc	ctcaacttga	caactcaaat	aatattttata	aatacagcca	cactttaaatt	165900
gggtcccat	tgaaatacat	atttaaatat	ctatacagtg	tgtaaaacc	aagaaaatat	165960
ttgattcttc	tctgatattt	aagaattgaa	ggtttgaggt	agttacgtgt	taggggcatt	166020
tatattcatg	tttttagagt	ttgcttatac	aacttaatct	ttccttttca	gtgctttggg	166080

ctcctgggag	ttaatggggc	tggaaaatca	tcaactttca	agatgttaac	aggagatacc	166140
actgttacca	gaggagatgc	tttccttaac	aaaaataggt	gagaaaagaa	gtggcttgta	166200
ttttgctgca	aagactttgt	ttttaattta	tttaaagaaa	taggttggtta	tttttgatta	166260
cagtggtatt	tttagagttc	ataaaaaatgt	tgaatatatag	taaagggttaa	agaagcacat	166320
aaaatcatcc	atgatttcaa	tatctagaga	taatcacaat	ttacatttcc	tttcagtctc	166380
attctcttct	tttaacagct	ttatttcaggt	ataattttaca	tacaatataa	tttgcttggt	166440
ttttaagagt	ataatttagt	gattttttggt	aaattgagag	ttttgcaacc	atcaccacaa	166500
tccagtttta	gaactttttcc	atcacccccc	atctgtctta	tatacacata	taaattgtgcc	166560
atacaattga	gatcatactg	tatgtagaat	ttaaaattag	tttttattgt	taatgagtgt	166620
attatgaata	tttccagtg	ggttacattt	cctaagatgt	ggaattttac	attgctacat	166680
aaaatccccc	tatgtacatg	tacctataat	ttattttaata	aattccttat	aaatgttgga	166740
cacattagtt	tccatttttc	actatgtaaa	tatgtccctg	tatacatctt	ttattatttc	166800
ctcaggaaca	attcctacaa	agtaaattgc	cctctctaaa	gagcatacaa	attgactgag	166860
ccaccgttag	gccattttct	gagactgcac	aggtcacaaa	gcaatctgat	ctttgggaat	166920
acagctacat	tttataggct	tcttagataa	tgttactcta	agtacttta	atatgtgggg	166980
cttctctggg	cttttttttt	tttgagacgg	agtttctactc	ttactgcccc	ggctggagag	167040
caatggcgcg	accttggtctc	actgcaacct	ccgcctccca	ggttcaagcg	attctcctgc	167100
ctcagcctcc	tgagtagctg	agattacagg	tgcccggccc	aatgcctgcc	taattttttt	167160
gtattttcag	tagagatggg	gtttcaccat	gttggccaga	ctggtctcga	gctcctgacc	167220
tcaggtgac	cacctgcctc	agcctcccaa	agtctctggga	ttacaggcat	gagccatgc	167280
gccccgcttc	tctggactta	ttatgtggag	agatagtaca	aggcagtggtc	tttcagagtt	167340
ttttgaccat	gaccgttggtg	ggaaatacat	tttatatctc	aacctagtat	gtacacacag	167400
acatgtagac	acatgtataa	cctaaagttt	cataaagcag	tacctactgt	tactaattgt	167460
agtgactct	gctattttct	attctacctt	atactcgctc	attaaaaaag	tgctggctcat	167520
gaccactaa	atatttttcc	caaaccacta	atgaacaatg	actcacaatt	tgaacacact	167580
ggacaggggg	atagccaata	aaattgaaaa	gagcaaggaa	attaatgtat	tcatgatctc	167640
ctctcctgtc	tcttacattt	ttgcagtagc	aatgtaaagg	aatcctaaga	gaacagacat	167700
tctgggaata	gcaggcctag	cgctgcacaa	ctgctttcct	aggcttgctc	ctagtaccaa	167760
gctcctgacg	catatagcag	tggcagtaat	aaccagccca	tagtaagggtt	tgctcacaggg	167820
actggttgta	agaactgatt	tggttggtat	agctgtgagg	gcctggcacg	gtgtccacgt	167880
gtgcctcaat	cctaattctg	aaaaaggctg	accctggggg	tgctaattag	atacacagag	167940
aggaatgaat	gctgccagaa	ggccaagttc	atggcaatgc	cgctgtggct	gaggtgcagt	168000
catcagctctg	gaacgtgaac	actgaacttc	tctcacatgt	gattcttcac	ttgactggat	168060
tcatagaacc	ccaaagccac	cccaccacca	cataaattgt	gtctctaggt	tctgtgttgc	168120
tcacactcaa	aattttctggg	ccttctcatt	tggtgcatgt	gaatggtgca	tatgagttaa	168180
gtctaggatg	gggccttagc	gttaaagccc	tggggtagtg	tgactgagat	tggttggtaaa	168240
gaatgtgcag	tggttggtcat	gacctcagaa	attctgaaat	gggactgcac	ctgcagactg	168300
aagtgttcag	agagccaggg	aggtgcaagg	actggggagg	gtagaggcag	gaaccctgcc	168360
tgccaggaag	agctagcatc	ctgggggcag	aaaggctgtg	ctttcaagta	gcagcagatg	168420
tattggtatc	tttgtaatgg	agaagcatac	tttacaggaa	cattaggcca	gattgtctaa	168480
ccagagtatc	tctacctgct	taaaatctaa	gtagttttct	tgctccttgc	agtatcttat	168540
caaacatcca	tgaagtacat	cagaacatgg	gctactgccc	tcagtttgat	gccatcacag	168600
agctgttgac	tgggagagaa	cacgtggagt	tctttgccct	tttgagagga	gtcccagaga	168660
aagaagtgg	caagggtactg	tgggcacctg	aaagccagcc	tgctctcctt	ggcatcctga	168720
caatatatac	cttatggctt	ttccacacgc	attgacttca	ggctgttttt	cctcatgaat	168780
gcagcagcac	aaaatgctgg	ttctttgtat	ctgctttcag	ggtggaacc	tgtaacggtg	168840
gtggggcagg	gctgggtggg	cagagaggga	gtgctgctcc	caccacacga	gtcccttctc	168900
cctgctttgg	ctcctcacca	gttgctcaggt	tatgattata	gaatctagtc	ctactcagtg	168960
aaagaacttt	catacatgta	tgtgtaggac	agcatgataa	aattcccaag	ccagaccaaa	169020
gtcaagggtc	tttttatcac	tgtagggttg	tgagtgggcg	attcggaac	tgggcctcgt	169080
gaagtatgga	gaaaaatatg	ctggttaacta	tagtggaggc	aacaaacgca	agctctctac	169140
agccatggct	ttgatcggc	ggcctcctgt	ggtgtttctg	gtgagtataa	ctgtggatgg	169200
aaaactggtg	ttctggcctg	agtggaaaac	atgactgttc	aaaagtccca	tatgtccagg	169260
gctgtgtgat	gattggcttg	tcttccccc	gggacagcag	agcaaccttg	gaaaagcaga	169320

gggaagcttc	tccttggca	cacactggg	tggtgtacc	atgcctgcag	atgctcccaa	169380
atagaggcac	tccaagcact	ttgtttctta	gcgtgattga	ggctggatat	gtgatttgat	169440
ctttctctgg	aacattcttt	ctaactcatct	ttgtgttcat	tccttgaaaa	tgaagagtgt	169500
ggacacagct	ttaaaatccc	caaggttagca	actaggtcat	agttcctnta	cacacggata	169560
gatgaaaaac	agatcagact	gggaagtggc	ccttgacctt	ttttctctg	tagataaagag	169620
cattgatggt	attacgggaa	gaagcctttg	aggcttttat	gtattccacc	tcggctcggg	169680
atgtgtttct	gtaaggctaa	cagttgcaat	atactagggt	aatctgagt	agctggaatt	169740
aaaaaaaaaa	aggaatttca	ccccaatctt	atactgactt	caatagagg	ttcagacaaa	169800
aagtgtttt	gtatatactt	atcagtcagt	aaaagataat	tacaactaaa	tggccttttt	169860
ccttccctat	ttatttggag	aaattttaatt	acataaaaaa	gtactcagaa	tatttgagtt	169920
tcctgcata	ataagacatt	tataataatg	accttgttta	caaataaatt	tgaagttac	169980
tctaattctt	tgattcatca	agaaataact	agaatggcaa	gttaaaattt	aagctgtttc	170040
aaagatgctt	ctgcatttaa	aaacaaattt	atctttgatt	ttttttcccc	ccagcaata	170100
agacttattt	tattctaatt	acaggatgaa	cccaccacag	gcattggatcc	caaagcccg	170160
cggttcttgt	ggaattgtgc	cctaagtgtt	gtcaaggagg	ggagatcagt	agtgcttaca	170220
tctcataggt	ccgtagttaa	gtcttgggtt	cctcactgtg	ggatgtttta	actttccaag	170280
tagaatatgc	gatcattttg	taaaaattag	aaaatacaga	aaagcaaaga	gtaaaaaat	170340
tattacctga	aattatata	gcataattctt	acaaaaatgc	aagccagta	taaatactgc	170400
tctttttcac	ttaatatatt	gtaaacatta	ttccaagtca	gtgcatttag	gtgcttttc	170460
ttatagctgg	atagtattcc	attaggatat	actcttattt	aactattccc	cctttttag	170520
acatttggat	tatttccaac	ttgttcacaa	ttgtaaacac	cactacactg	aacagcatca	170580
tccttatatc	cacatgtact	tgtaacagaa	tacaattccc	taggaagctg	gaatgctgga	170640
agtcattggt	atgttctcat	ggttacagag	aatctctcta	aaactaaaac	ctctttctgt	170700
tttaccgcag	tatggaagaa	tgtgaagctc	tttgcactag	gatggcaatc	atggtcaatg	170760
gaaggttccag	gtgccttggc	agtgtccagc	atctaaaaaa	taggtaataa	agataatttc	170820
tttgggatag	tgctagtga	gaaggcttga	tattttattct	tttgtgagta	tataaatggt	170880
gcctctaaaa	taaagggaaa	taaaactgag	caaaacagta	tagtggaag	aatgagggct	170940
ttgaagtccg	aactgcattc	aaattctgtc	tttaccattt	actggttctg	tgactcttgg	171000
gcaagtctact	taactactgt	aagagttagt	ttccctggaa	gatctacctc	ctagctttgt	171060
gctatagatg	aaatgaaaaa	aattttacatg	tgccagtact	ggtgagagcg	caagcttttg	171120
agtcaaacac	aaatgggttt	gcattcctggc	cctaccaatt	atgagctctg	agccatgggc	171180
aagtgaactaa	ctccctgggc	ctcagtttct	ctgtaacatc	tgtcagactt	catgggtcca	171240
ggtgaggatt	aaaggagatc	atgtattttc	agcactatggc	atggtgcttc	acataaaaata	171300
agtatttagt	aaatgataac	tggttccctc	tctcagaaac	ttatttctgg	gcctgccagg	171360
ggccgccctt	tttcatggca	caagttgggt	tcacagggtt	cagtattctt	ttaaatagtt	171420
ttctggagat	cctccatttg	ggtatttttt	cctgctttca	ggtttggaga	tggttatata	171480
atagtgttac	gaatagcagg	gtccaaccgc	gacctgaagc	ctgtccagga	tttctttgga	171540
cttgcatctc	ctggaagtgt	tctaaaagag	aaacaccgga	acatgctaca	ataccagctt	171600
ccatcttcat	tatcttctct	ggccaggata	ttcagcatcc	tctcccagag	caaaaagcga	171660
ctccacatag	aagactactc	tgtttctcag	acaacacttg	accaagtaag	ctttgagtgt	171720
caaaacagat	ttacttctca	gggtgtggat	tcctgccccg	acactcccgc	ccataggctc	171780
aagagcagtt	tgtatcttga	attgggtgctt	gaattcctga	tctactattc	ctagctatgc	171840
tttttactaa	acctctctga	acctgaaaag	ggagatgatg	cctatgtact	ctataggatt	171900
attgtgagaa	tttactgtaa	taataaccat	aaaaactacc	atttagtgag	cacctaccat	171960
gggcccaggca	ttttacttgg	tgccaaatcc	tattttaaatt	agataaaaaa	gtaccaaata	172020
ggtcctgaca	cttaagaagt	actcagtaaa	tattttcttc	cctcttccct	ttaatcaaga	172080
ccgtatgtgc	caaagtaaat	ggatgactga	gcagtgggtg	atgtaggggt	ggggggcgat	172140
atagaaaagtc	agtttttggc	cgggcgtggt	ggctcatgcc	tgtaatccca	gcactttggg	172200
aggctgagga	gcaggcagat	catgagggtca	ggagatccag	ataatcctgg	ccaacagggt	172260
gaaaccccg	ctctactaaa	aatacaaaaa	ttagctgggc	atggtgggtg	gcactttag	172320
tcacagctac	ttgcgaggct	gaggcaggag	aattgctcga	accaggagg	tggaggttac	172380
agtgagccaa	ggtctcgcca	ctgcactcc	gcctggggac	agagcaagac	cccatttcaa	172440
ggggggaaaa	aaagtctatt	tttaagttgt	tattgctttt	ttcaagtatt	cttccctcct	172500
tcacacacag	ttttctagtt	aatccattta	tgtaattctg	tatgctccta	cttgacctaa	172560

tttcaacatc	tggaataata	gaactagaat	aaagaatgag	caagttgagt	ggtatattata	172620
aaggtccatc	ttaatctttt	aacaggtatt	tgtgaacttt	gccaaaggacc	aaagtgatga	172680
tgaccactta	aaagacctct	cattacacaa	aaaccagaca	gtagtggacg	ttgcagttct	172740
cacatctttt	ctacaggatg	agaaagtga	agaaagctat	gtatgaagaa	tcctgttcat	172800
acgggggtggc	tgaaagttaa	gaggaactag	actttccctt	gcaccatgtg	aagtgttggtg	172860
gagaaaagag	ccagaagttg	atgtgggaag	aagttaaactg	gatactgtac	tgatactatt	172920
caatgcaatg	caattcaatg	caatgaaaac	aaaattccat	tacaggggca	gtgcctttgt	172980
agcctatgtc	ttgtatggct	ctcaagtga	agacttgaat	ttagtttttt	acctataacct	173040
atgtgaaact	ctattatgga	acccaatgga	catatgggtt	tgaactcaca	cttttttttt	173100
ttttttttgtt	cctgtgtatt	ctcattgggg	ttgcaacaat	aattcatcaa	gtaatcatgg	173160
ccagcgatta	ttgatcaaaa	tcaaaaggta	atgcacatcc	tcattcacta	agccatgcca	173220
tgcccaggag	actggtttcc	cggtgacaca	tccattgctg	gcaatgagtg	tgccagagtt	173280
attagtgcga	agtttttccag	aaagtttgaa	gcaccatggt	gtgtcatgct	cacttttgtg	173340
aaagctgctc	tgctcagagt	ctatcaacat	tgaatatcag	ttgacagaat	ggtgccatgc	173400
gtggctaaca	tcctgttttg	attccctctg	ataagctggt	ctgggtggcag	taacatgcaa	173460
caaaaatgtg	gggtgtctcca	ggcacgggaa	acttggttcc	attgtttatat	tgctctatgc	173520
ttcgagccat	gggtctacag	ggtcatcctt	atgagactct	taaatatact	tagatcctgg	173580
taagaggcaa	agaatcaaca	gccaaactgc	tggggctgca	agctgctgaa	gccagggcat	173640
gggattaaag	agattgtgcg	ttcaaactca	gggaagcctg	tgcccatttg	tcctgactgt	173700
ctgctaacat	ggtagactgc	atctcaagat	gtttatctga	cacaagtgtg	ttatttctgg	173760
ctttttgaat	taatctagaa	aatgaaaaga	tggagtgtga	ttttgacaaa	aatgtttgta	173820
cttttttaatg	ttatttggaa	ttttaagttc	tatcagtgac	ttctgaatcc	ttagaatggc	173880
ctctttgtag	aaccctgtgg	tatagaggag	tatggccact	gccccactat	ttttattttc	173940
ttatgtaagt	ttgcatatca	gtcatgacta	gtgcctagaa	agcaatgtga	tggtcaggat	174000
ctcatgacan	ttatatattga	gtttctttca	gatcatttag	gatactctta	atctcacttc	174060
atcaatcaaa	tattttttga	gtgtatgctg	tagctgaaag	agtatgtacg	tacgtataag	174120
actagagaga	tattaagtct	cagtacactt	cctgtgccat	gttattcagc	tcactgggtt	174180
acaaatatag	ggtgtcttgt	ggtgttagga	gccactgta	acaatactgg	gcagcctttt	174240
tttttttttt	tttaattgca	acaatgcaaa	agccaagaaa	gtataagggt	cacaagtcta	174300
aacaatgaat	tcnttcaaca	gggaaaacag	ctagcttgaa	aacttgctga	aaaacacaa	174360
ttgtgtttat	ggcattttag	accttcaaat	aattggcttt	gcagatattg	gatacccat	174420
taaatctgac	agtctcaaat	ttttcatctc	ttcaatcact	agtcaagaaa	aatataaaaa	174480
caacaaatca	ttccatatgg	agcatttttc	agagtttttc	aacctgctct	tatttttcta	174540
gtcagtaaac	atgtgtaaaa	atactgtttc	actaatactt	actgttaact	gtcttgagag	174600
aaaagaaaaa	tatgagagaa	ctattgtttg	gggaagttca	agtgatcttt	caatatcatt	174660
actaaactct	tcactttttt	ccagaatttg	aatattaacg	ctaaagggtg	aagacttcag	174720
atttcaaatt	aatcttttcta	tattttttta	atltacagaa	tattatataa	cccactgctg	174780
aaaaagaaaa	aatgatttgt	tttagaagtt	aaagtcaata	ttgattttta	atataagtaa	174840
tgaaggcata	tttccaataa	ctagtgatat	ggcatcggtg	catttttacag	tatcttcaaa	174900
aatacagaat	ttatagaata	atttctctct	atttaatat	tttcaaaatc	aaagttatgg	174960
tttctctcatt	ttactaaaa	cgtattctaa	ttcttcatta	tagtaaatct	atgagcaact	175020
ccttacttctg	gttccctctga	tttcaaggcc	atatttttaa	aaatcaaaaag	gcactgtgaa	175080
ctatttttgaa	gaaaacacaa	catttttaata	cagattgaaa	ggacctcttc	tgaagctaga	175140
aacaatctat	agttatacat	cttcattaat	actgtgttac	cttttaaaat	agtaattttt	175200
tacatttttcc	tgtgtaaacc	taattgtggg	agaaattttt	accaactcta	tactcaatca	175260
agcaaaattt	ctgtatatct	cctgtggaat	gtacctatgt	gagtttcaga	aattctcaaa	175320
atacgtgttc	aaaaatttct	gcttttgcat	ctttgggaca	cctcagaaaa	cttattaaca	175380
actgtgaata	tgagaaatac	agaagaaaa	aataagccct	ctatacataa	atgcccagca	175440
caattcattg	ttaaaaaaca	accaaaccct	acactactgt	atttcattat	ctgtactgaa	175500
agcaaatgct	ttgtgactat	taaaatgttc	acatcattca	ttcactgtat	agtaatcatt	175560
gactaaagcc	atgtgtctgt	gttttcttct	tgtgggtgta	tatatcaggt	aaaatatttt	175620
ccaaagagcc	atgtgtcatg	taatactgaa	ccactttgat	attgagacat	taatttgtac	175680
cctgtgttatt	atctactagt	aataatgtaa	tactgtagaa	atattgctct	aattcttttc	175740
aaaattgttg	catccccctt	agaatgtttc	tatttccata	aggatttagg	tatgctatta	175800

tcccttctta	taccctaaga	tgaagctggt	tktgtgctct	ttgttcatca	ttggccctca	175860
ttccaagcac	tttacgctgt	ctgtaatgsg	atctatTTTT	gcactgggaat	atctgagaaa	175920
rtgmamaact	agacaaaagt	ttcacaaacag	atcttctaagt	taaatacattt	tcatawaaarr	175980
raaaararaa	aaaaaatttt	gtatgtcaat	aactttatat	gaagtattaa	aatgcattat	176040
tctatgttgt	aataataatga	gtcacaaaat	aaagctgtga	cagttctggt	ggtctacaga	176100
aatttacttt	tgtgcatttg	tggcaccacc	tactgttgaa	gggttataaa	gccattagaa	176160
aagtagaggg	gaagtgattt	ggatcaaaag	gaaaaaacttt	agaaaagatt	caaatgttcc	176220
cttaatcata	aaagagaact	gaggggacta	cttgaaaata	aaaggttggt	ttgtattttc	176280
atgttggtta	agatactgag	ntaacwggta	ttaagtgtta	gaggttttta	gataaatatt	176340
ctgcttaatg	attatgaagc	tgcactgaga	tttctgaaaa	tgctctgtag	ctgagcttat	176400
ttaataaatg	ttcacttggt	ataggggaag	ctacaaaggc	agccttcagt	gtccttttgt	176460
ttattcaacc	aaaaatataa	ggacacaatg	tagcagttat	actgggaagg	tgctgggggt	176520
ggtggcaatg	gtgagcagga	aggcgaagta	gatattggaa	cagaaatgat	actaatatcg	176580
gtgattcctt	ccttttttcc	tgtrataagt	gtgtgtcaga	caacatatga	gcagtgtctga	176640
taaatgtaaa	tgtattkttc	atagctcatt	aagaatcagt	ttcagaaaga	gatgtctgct	176700
tatttkgctr	cttgaagaat	ccctgtcaaa	cagtcctttt	saggaagtac	aagaggctgt	176760
ctctattttg	gacctcagga	atggctgtga	cagtgctgtg	agcagtcctt	ttcctgtggc	176820
acagatctga	actttgtgtg	cagaaaaatc	ttggcttcaa	gtgagccaag	atgccccctg	176880
agcatcagca	tcacaacttc	atcctcctat	cttgaagttc	atgttatagt	gactttaatg	176940
aaatcataga	acactgtttc	ttcgtgnaac	aatgacgagg	gagaggaaaa	aactttattg	177000
aaaaataaaa	aggcaggtaa	tttagatgaa	aatatgttac	ccatgagggt	ttgtttttgc	177060
tttttgtttt	tgttttttgag	aaacagaatc	tcgctctgtc	gtccaggctg	gagtgcagcg	177120
gcatgatctt	ggctcactgc	aacctccgcc	tcccgggttc	aagcgattct	cctcagcttc	177180
ccaagtagct	ggtactacag	gcattgcgcca	ccacaaccag	ctaatttttg	tatttttagt	177240
agagatgggg	tttactata	cgttgccag	gctggtctca	aactcctgac	ctaagggtgat	177300
ccttctgcct	tgggtcocca	aagtgtctgg	attacaggca	tgagccacct	tgccctggccc	177360
tacctatgag	ccttgactaa	aacattcttc	tatctgtaga	aaagcccaaa	agaacttttc	177420
cagattcaaa	aaacttggca	ctttgtaatg	gtaatgttta	cattaagtaa	aaaaaaaaaa	177480
aaaaccact	tagcttcagt	tttcaagtgt	ttactgtgtt	gtcatgcact	tcatttaatt	177540
ctcaacacct	gccctatgag	gtaaaaagta	ccattttaca	tatgagtaaa	ttacagctca	177600
gtggataaga	aactcgtcca	aaggtacagg	ttcagtcagg	tggcagaggg	ttctttttgt	177660
tgaagttagg	tatcagttaa	aattgacctt	gtaaaaatc	atcagcatca	atataattat	177720
atgttaacaaa	tattttatga	actttactgt	atgccagata	cttctctagg	tactaggggg	177780
tacaatgtag	aagaaaatag	aattcctgct	ctaataaatt	tatatattcag	tgggtgaaaga	177840
tgatgtgtgg	acaaacacat	ctaattgtatt	ttgacagcaa	tgggtgtctaa	gaagaaaata	177900
agacatggta	attggataac	aatggagaga	agtcagagat	ggcctttttc	gaggagtgc	177960
atgctcagaa	tcgaataaaa	agagcaggag	cagcctttca	aggtgggtgc	gaaggatatt	178020
cccgaagaa	agaataagtg	ttgcaaaagc	cccagtgagg	aaaagcttgg	caagctgagg	178080
tggtaaaaga	gctatctgta	ctaattgtctc	ttgtactgag	ttagcaagga	caagagtggc	178140
aggggggtgga	actggagaga	tagcagggac	cacatctcac	aggatctcgc	cagccttttt	178200
aaggattttg	gattttattg	ttagtgcaac	aaggagccac	tggagagttt	taaacagtag	178260
tgggtgtgacc	tactgtttca	gaaagaacac	tggctactat	gggaagaaag	gacagttaga	178320
agactaatag	ataatgggtg	attgaactaa	gatggtagca	acagataggg	agctatggta	178380
atgttcagta	tccacttttg	agatagatcc	agcaggactt	gctgacagac	tgcatgtaa	178440
ggctgagggga	aagagagcta	gcaagggtgac	ttctagtttg	tgacctgaac	taggttagatg	178500
gttgtgttaa	aaatgcagtg	ggtattttcag	tctgaagctc	agggggcaatg	atggaaaata	178560
agataaatgt	gtgcaagtgt	gctgggcgtg	gtgggtgcacg	cctataatca	cagcactttg	178620
ggaggccgag	acgggtggat	cacttgagggt	caggcgtttg	cgaccagcct	aacatgggtga	178680
aaccccatct	ctaataaata	caaaaaaatt	agctgggcat	ggtggtgcat	gcctgtaatc	178740
caagctactt	gggaggctga	gacaagagaa	tcgcttgcac	ctgggaggcg	gaggtttcag	178800
tgagctgaga	tcgcaccatt	gcactccagc	ctgggcaaca	agagcgaaac	tccatctaaa	178860
aaaaaaagtg	tgcaagttat	tggtaactgt	atatttaagc	ctcgggactg	aatgagatta	178920
cctagagaga	atgaagatag	ggaacattct	tgagcctgag	atcctataac	atttagaaga	178980
gaagctagcc	agggaattg	agagggactg	gccagtgaga	gagagtaaaa	tctgaagagt	179040

ataatgccat	atgttgaagc	tcagagaatt	attgtttcag	gaaggcagaa	gttgtaatt	179100
atgtccaaca	ttgctgagaa	gatgagtaag	gaatgtaa	gagtaaaggc	aggaatggct	179160
attgaatttg	ttaagacaga	ggtccttggt	gaccttccta	agagtcattt	cagcatgaca	179220
aggatgcaga	cctaactgga	atagattttc	aggggaagact	gagaggcaag	gaaggggaga	179280
ctgcaaata	atgcaaatct	atattttttgc	tttgaaggga	aacagaaaa	aggacaacag	179340
ctgggtttaca	gaacttttat	ttggattctt	tccttgctcg	ttaataatat	aggctgcacc	179400
tgggcatcat	cgtgcccttc	ctttttgatt	ctgctgtttt	gcttttaatc	ctacaggcat	179460
ttcttctggc	aggagccttg	tacacactct	gggtggttca	tgaccaccac	ggacttgccc	179520
tttcaaggca	gaagcctgtg	attcaaaaa	ttccattcct	tccaatcgac	tattataaaa	179580
ctcaatttgt	ctagtgccca	tactccttta	ccttaggac	ctgggccaac	tgctagata	179640
gaaaacaaac	catttcctcc	tcctggggga	atgtgcttct	ttcaagaagg	tgcttagaga	179700
atagacattc	taggtgacag	cagttatgaa	agaggtgtct	ctaatagaac	taacacttct	179760
tccaacatac	tocaggttca	ccctcctttg	aagacagaaa	gtactacaac	ttcagttgcc	179820
accctagtca	ggttcatagg	atttactcag	taggttaaga	gatggtgctg	agaatgaagt	179880
ccagagtttg	agtctacaag	tggcatttgc	ttctcctttg	ggacttctgt	ggcagggtgt	179940
ggaaccaa	cagattgggt	gcatatctgt	ttctcttct	gaaaatacaa	ttcaaatacc	180000
ttcatagtct	gtgacagcaa	cttataacca	acagacaatg	gtattatttt	tatttattga	180060
tggcactccc	ccatagccag	aacttctact	gagtcattca	tcgtgtattc	caggaatact	180120
ttccaaatgg	agtagtgagg	cacttccaat	aacagttatg	taatctgtta	acagtggctc	180180
aaaatgacat	gtgaaggaa	gatgtacttc	ttttttcaga	ctcacagatc	tcatatgtta	180240
attcagtcaa	caagtactta	gggcttatca	catgccaggc	acaggtaata	tgacaataat	180300
gaaaacaaaa	acccttgctg	tcatagaatt	cgttttctag	tgggaagaga	catacatata	180360
caaatcatat	ataagtaaaa	cattaattat	ggtgataaca	gaaaaagaaa	gcaggggaga	180420
gggtagtggt	cttagttcag	gttgctgtaa	caagagtacc	atagacaggg	tggcttamac	180480
aacaaacatt	tccttctcac	agatctagt	gctgggaagt	ctaagaccag	ggtgccagca	180540
tgaagaagtt	ctgggtgaagg	cttacattct	ggttctctca	cagtgaaggc	tcctcacgcc	180600
cttataaaatg	cactaattct	attaccacac	tgacctcatc	taaaactaac	tcacaaaggc	180660
caaacctcct	atgttgagat	taaggcttca	acataggaat	tttgggggga	caaaaacatt	180720
cagtctctag	cagatagggg	ccactgtggg	aggggattac	aatcttaaat	agggttgtca	180780
gggaaggcct	catgagggca	aagacctgag	gaggcatgga	aatgatccac	gcagatgcat	180840
gtctggggaa	gagcattcca	ggcagaggca	gtgggaatgg	accctcagg	aagagcatgt	180900
ttagcaagtt	cagagaaaag	cctcttaggt	caggtctgga	gcgagagtgg	aaaatgtaac	180960
aggacagatc	atgtaaagac	ttgtagacca	cagttagagg	cttggaacat	aactctgagg	181020
atgacatgaa	gggtattgga	gggggtgttg	agcagaggag	tgatatgac	tggtttatat	181080
tttagattat	tctgactgct	atgttgaaaa	taggggtgag	agcagagggg	aagggcagca	181140
caccagttaa	gaccacttcc	caaaaatcca	gatgatgatg	ggcttgaacc	aggagagttg	181200
ctatagggat	gtgaagcaat	caaattctag	atatattggga	cctgctgaca	ggtacataat	181260
ggtgtatgag	agaaaaggca	gtgtgagaat	gactctgaag	tctgtggcct	gagcaaaa	181320
gaaacctgga	gttgccaata	gctgagataa	agtttctggt	taaagatcaa	gagctcagtt	181380
ttggacaaga	ggggtgtgag	atttctaata	gacattcagg	tggaggtgtg	gggaacacac	181440
ctggatgtga	tgagcctgga	attcaaatc	acatgtgtga	atttgaaaaa	agattcagaa	181500
aagaggtgtg	gactggagga	gctatccaca	cacagatagc	atttgaagcc	acaagactgg	181560
gggtgatgac	gcagggaagta	agtataaata	gaaaagagaa	gtggtccaag	gactcagtc	181620
ttacatcaga	ggtcaaagag	acaagatgga	gactaggaga	tatgaaggct	tatgcagtga	181680
gtgtttcgga	gaaacgaaga	aacttcccag	aagaaaggag	aggtcaactg	ctaacaagtc	181740
aagtgaatg	agaactggga	aatgagttga	caagagcaat	ttggtctggc	tgatcagaga	181800
atgtttaaga	gataatgtga	gggaagaaaa	tggaggcagg	aagtatgaac	tactctttg	181860
agtcataattg	taaaggaaaa	aaatggggtg	attttactct	ttttttttt	taaagatagg	181920
aaaaaaaaagt	atatttatat	gctgaggaga	agaatccagt	tgaaggggaa	tactgtggct	181980
tcaggagaca	ggaaaactgc	ctaagccaca	tccttcagca	agtgaagtgt	caagtggagg	182040
gtttgtcttt	gcttggggca	cgggctgttc	atccacagtg	aaaggagaga	aggcagggca	182100
tgtgggggtg	gctgtagaaa	gcgggagagc	ggggtgggaa	cttatgaaga	ctcttctgnt	182160
tgttattttc	tctgttaagt	aaaaggaaa	gtcattggct	aagaatgaag	atggacgcgc	182220
aggtgctggg	agtcacagaa	gagaatgaaa	gaatgaataa	aatagagaaa	aatacaatgc	182280

```

tattatataa acctatacat tttaaattact ttcctcttca aattagaccc cctggaaggc 182340
aaatctctgt catgttaagt tttaggaaaa gtcataatct acttggagct aagtatgaag 182400
aataagggtat atgattttaa ccacataatt ctatttttgc ttaaaccggg gaagccttta 182460
aggtaacgta gagtgtaacc attaaaaaag ataaaaatgt cagcttcccc ttccctttta 182520
atatagtaag gctcaaagggt aattgatggt cataacccta aggtactata acagtctgaa 182580
gcaaaatatt aaatgtcttc tgtagtattt tagttaactt ttaattttat tggtaattta 182640
tgtgtagtta accacatact tgtgcctcaa ctatttcaca taaatgtgag atgtcttagg 182700
cctctttgaa ctctgcatgg aaaagaatgc tgaggaggta tgtctgttta agctgccact 182760
gctgcctct cataaataat atctcacatt gcataatagc ccagataaac tgcagatcgc 182820
ttagagcctg ataaatgaga ggaaactgta cagtttggtt tccaaattgc ccttggacag 182880
ctaattcaca atttactatt ttatagctgt aagattttta aaatataaaa taacatagct 182940
gtaaatacag attatcagaa gatagtctgt aaaaaatgtaa atataatata gctgtaaata 183000
tacactatcg gaagtaccaa atctagtttt agtaggtaga ggcatacagt aaaatggaaa 183060
tgaaagatgt ttcaaggaaa actccaggac atctgtggca gtactaaaga aaccttcctt 183120
ctcaggttcc cagcatgcta ttttattgat gtaacaacat tttcaataaa gttgggtaaat 183180
tatcactata ttactgtctt atagcaacat agcaagagct ttagagatca tataagtata 183240
aaatgtgaat ttaaaaaaac aatgaatatg caggattttt attagggcaa gcgtttccat 183300
aaccataaat atttctttta aacaaataaa tgtcccaaga tctctgttag tgatccaaac 183360
taagttagaa ttagtataat taattataaa tgaacaattt cagcatataa accaacaagt 183420
cttttctaga tttttaacac tgtgacccaa ttgcattatt ttccaagtta gaatgactaa 183480
taatcaatga atgtaaaagc aataattaat acagatgaca ttgtactttt ccacagtaaa 183540
gaaataaaca atctaataat tttataaatc ccattttata tcacaaaata acctttacta 183600
agcaaatttt tttaaaatct caggaaactat agacatgatg aaaagataga tattttatat 183660
aaataattca aaaatactgt caggcaagga aatgtaaaaat ccttatttga gtaaaagaaa 183720
atgctataaa gcaatgagtt atcaaaatac agaagaggta ttctaaaaca aatgaaaaac 183780
caagatgatg aaatagtgac aactacttct aatgtgtaac agatactgaa atgccaaggt 183840
gaaagtgaac tgaattattt cttaaagcag tggagaatat gtaactttca aaaatgcaag 183900
aagcacagca aattaactaa ttaacttacc acctccttca aataaaaagcg agaacctctt 183960
gggagaattt aagcaccatt agcagacaca tcttagagc 183999

```

<210> 2
 <211> 21
 <212> DNA
 <213> homo sapien

<400> 2
 ggaagtgttc taaaagagaa a 21

<210> 3
 <211> 21
 <212> DNA
 <213> homo sapien

<400> 3
 agtaaagagg gactagactt t 21

<210> 4
 <211> 21
 <212> DNA
 <213> homo sapien

<400> 4
agtaaagagg aactagactt t

21

<210> 5
<211> 2261
<212> PRT
<213> homo sapien

<400> 5
Met Ala Cys Trp Pro Gln Leu Arg Leu Leu Leu Trp Lys Asn Leu Thr
1 5 10 15
Phe Arg Arg Arg Gln Thr Cys Gln Leu Leu Leu Glu Val Ala Trp Pro
20 25 30
Leu Phe Ile Phe Leu Ile Leu Ile Ser Val Arg Leu Ser Tyr Pro Pro
35 40 45
Tyr Glu Gln His Glu Cys His Phe Pro Asn Lys Ala Met Pro Ser Ala
50 55 60
Gly Thr Leu Pro Trp Val Gln Gly Ile Ile Cys Asn Ala Asn Asn Pro
65 70 75 80
Cys Phe Arg Tyr Pro Thr Pro Gly Glu Ala Pro Gly Val Val Gly Asn
85 90 95
Phe Asn Lys Ser Ile Val Ala Arg Leu Phe Ser Asp Ala Arg Arg Leu
100 105 110
Leu Leu Tyr Ser Gln Lys Asp Thr Ser Met Lys Asp Met Arg Lys Val
115 120 125
Leu Arg Thr Leu Gln Gln Ile Lys Lys Ser Ser Ser Asn Leu Lys Leu
130 135 140
Gln Asp Phe Leu Val Asp Asn Glu Thr Phe Ser Gly Phe Leu Tyr His
145 150 155 160
Asn Leu Ser Leu Pro Lys Ser Thr Val Asp Lys Met Leu Arg Ala Asp
165 170 175
Val Ile Leu His Lys Val Phe Leu Gln Gly Tyr Gln Leu His Leu Thr
180 185 190
Ser Leu Cys Asn Gly Ser Lys Ser Glu Glu Met Ile Gln Leu Gly Asp
195 200 205
Gln Glu Val Ser Glu Leu Cys Gly Leu Pro Arg Glu Lys Leu Ala Ala
210 215 220
Ala Glu Arg Val Leu Arg Ser Asn Met Asp Ile Leu Lys Pro Ile Leu
225 230 235 240
Arg Thr Leu Asn Ser Thr Ser Pro Phe Pro Ser Lys Glu Leu Ala Glu
245 250 255
Ala Thr Lys Thr Leu Leu His Ser Leu Gly Thr Leu Ala Gln Glu Leu
260 265 270
Phe Ser Met Arg Ser Trp Ser Asp Met Arg Gln Glu Val Met Phe Leu
275 280 285
Thr Asn Val Asn Ser Ser Ser Ser Ser Thr Gln Ile Tyr Gln Ala Val
290 295 300
Ser Arg Ile Val Cys Gly His Pro Glu Gly Gly Gly Leu Lys Ile Lys
305 310 315 320
Ser Leu Asn Trp Tyr Glu Asp Asn Asn Tyr Lys Ala Leu Phe Gly Gly
325 330 335
Asn Gly Thr Glu Glu Asp Ala Glu Thr Phe Tyr Asp Asn Ser Thr Thr
340 345 350

Pro	Tyr	Cys	Asn	Asp	Leu	Met	Lys	Asn	Leu	Glu	Ser	Ser	Pro	Leu	Ser
		355					360					365			
Arg	Ile	Ile	Trp	Lys	Ala	Leu	Lys	Pro	Leu	Leu	Val	Gly	Lys	Ile	Leu
	370					375					380				
Tyr	Thr	Pro	Asp	Thr	Pro	Ala	Thr	Arg	Gln	Val	Met	Ala	Glu	Val	Asn
385					390					395					400
Lys	Thr	Phe	Gln	Glu	Leu	Ala	Val	Phe	His	Asp	Leu	Glu	Gly	Met	Trp
			405						410					415	
Glu	Glu	Leu	Ser	Pro	Lys	Ile	Trp	Thr	Phe	Met	Glu	Asn	Ser	Gln	Glu
			420					425					430		
Met	Asp	Leu	Val	Arg	Met	Leu	Leu	Asp	Ser	Arg	Asp	Asn	Asp	His	Phe
		435				440						445			
Trp	Glu	Gln	Gln	Leu	Asp	Gly	Leu	Asp	Trp	Thr	Ala	Gln	Asp	Ile	Val
	450					455					460				
Ala	Phe	Leu	Ala	Lys	His	Pro	Glu	Asp	Val	Gln	Ser	Ser	Asn	Gly	Ser
465					470					475					480
Val	Tyr	Thr	Trp	Arg	Glu	Ala	Phe	Asn	Glu	Thr	Asn	Gln	Ala	Ile	Arg
				485					490					495	
Thr	Ile	Ser	Arg	Phe	Met	Glu	Cys	Val	Asn	Leu	Asn	Lys	Leu	Glu	Pro
		500						505					510		
Ile	Ala	Thr	Glu	Val	Trp	Leu	Ile	Asn	Lys	Ser	Met	Glu	Leu	Leu	Asp
	515					520						525			
Glu	Arg	Lys	Phe	Trp	Ala	Gly	Ile	Val	Phe	Thr	Gly	Ile	Thr	Pro	Gly
	530					535					540				
Ser	Ile	Glu	Leu	Pro	His	His	Val	Lys	Tyr	Lys	Ile	Arg	Met	Asp	Ile
545					550					555					560
Asp	Asn	Val	Glu	Arg	Thr	Asn	Lys	Ile	Lys	Asp	Gly	Tyr	Trp	Asp	Pro
				565					570					575	
Gly	Pro	Arg	Ala	Asp	Pro	Phe	Glu	Asp	Met	Arg	Tyr	Val	Trp	Gly	Gly
			580					585					590		
Phe	Ala	Tyr	Leu	Gln	Asp	Val	Val	Glu	Gln	Ala	Ile	Ile	Arg	Val	Leu
	595					600						605			
Thr	Gly	Thr	Glu	Lys	Lys	Thr	Gly	Val	Tyr	Met	Gln	Gln	Met	Pro	Tyr
	610					615					620				
Pro	Cys	Tyr	Val	Asp	Asp	Ile	Phe	Leu	Arg	Val	Met	Ser	Arg	Ser	Met
625					630					635					640
Pro	Leu	Phe	Met	Thr	Leu	Ala	Trp	Ile	Tyr	Ser	Val	Ala	Val	Ile	Ile
				645					650					655	
Lys	Gly	Ile	Val	Tyr	Glu	Lys	Glu	Ala	Arg	Leu	Lys	Glu	Thr	Met	Arg
			660					665					670		
Ile	Met	Gly	Leu	Asp	Asn	Ser	Ile	Leu	Trp	Phe	Ser	Trp	Phe	Ile	Ser
	675						680					685			
Ser	Leu	Ile	Pro	Leu	Leu	Val	Ser	Ala	Gly	Leu	Leu	Val	Val	Ile	Leu
	690					695					700				
Lys	Leu	Gly	Asn	Leu	Leu	Pro	Tyr	Ser	Asp	Pro	Ser	Val	Val	Phe	Val
705					710					715					720
Phe	Leu	Ser	Val	Phe	Ala	Val	Val	Thr	Ile	Leu	Gln	Cys	Phe	Leu	Ile
				725					730					735	
Ser	Thr	Leu	Phe	Ser	Arg	Ala	Asn	Leu	Ala	Ala	Ala	Cys	Gly	Gly	Ile
			740				745					750			
Ile	Tyr	Phe	Thr	Leu	Tyr	Leu	Pro	Tyr	Val	Leu	Cys	Val	Ala	Trp	Gln
	755						760					765			
Asp	Tyr	Val	Gly	Phe	Thr	Leu	Lys	Ile	Phe	Ala	Ser	Leu	Leu	Ser	Pro
	770					775						780			

Val	Ala	Phe	Gly	Phe	Gly	Cys	Glu	Tyr	Phe	Ala	Leu	Phe	Glu	Glu	Gln
785					790					795					800
Gly	Ile	Gly	Val	Gln	Trp	Asp	Asn	Leu	Phe	Glu	Ser	Pro	Val	Glu	Glu
				805					810						815
Asp	Gly	Phe	Asn	Leu	Thr	Thr	Ser	Val	Ser	Met	Met	Leu	Phe	Asp	Thr
			820					825					830		
Phe	Leu	Tyr	Gly	Val	Met	Thr	Trp	Tyr	Ile	Glu	Ala	Val	Phe	Pro	Gly
		835					840					845			
Gln	Tyr	Gly	Ile	Pro	Arg	Pro	Trp	Tyr	Phe	Pro	Cys	Thr	Lys	Ser	Tyr
	850					855					860				
Trp	Phe	Gly	Glu	Glu	Ser	Asp	Glu	Lys	Ser	His	Pro	Gly	Ser	Asn	Gln
865					870					875					880
Lys	Arg	Ile	Ser	Glu	Ile	Cys	Met	Glu	Glu	Glu	Pro	Thr	His	Leu	Lys
				885					890					895	
Leu	Gly	Val	Ser	Ile	Gln	Asn	Leu	Val	Lys	Val	Tyr	Arg	Asp	Gly	Met
			900					905					910		
Lys	Val	Ala	Val	Asp	Gly	Leu	Ala	Leu	Asn	Phe	Tyr	Glu	Gly	Gln	Ile
		915					920					925			
Thr	Ser	Phe	Leu	Gly	His	Asn	Gly	Ala	Gly	Lys	Thr	Thr	Thr	Met	Ser
	930					935						940			
Ile	Leu	Thr	Gly	Leu	Phe	Pro	Pro	Thr	Ser	Gly	Thr	Ala	Tyr	Ile	Leu
945					950					955					960
Gly	Lys	Asp	Ile	Arg	Ser	Glu	Met	Ser	Thr	Ile	Arg	Gln	Asn	Leu	Gly
				965					970					975	
Val	Cys	Pro	Gln	His	Asn	Val	Leu	Phe	Asp	Met	Leu	Thr	Val	Glu	Glu
			980					985					990		
His	Ile	Trp	Phe	Tyr	Ala	Arg	Leu	Lys	Gly	Leu	Ser	Glu	Lys	His	Val
		995					1000					1005			
Lys	Ala	Glu	Met	Glu	Gln	Met	Ala	Leu	Asp	Val	Gly	Leu	Pro	Ser	Ser
	1010					1015					1020				
Lys	Leu	Lys	Ser	Lys	Thr	Ser	Gln	Leu	Ser	Gly	Gly	Met	Gln	Arg	Lys
1025					1030					1035					1040
Leu	Ser	Val	Ala	Leu	Ala	Phe	Val	Gly	Gly	Ser	Lys	Val	Val	Ile	Leu
				1045					1050					1055	
Asp	Glu	Pro	Thr	Ala	Gly	Val	Asp	Pro	Tyr	Ser	Arg	Arg	Gly	Ile	Trp
			1060					1065					1070		
Glu	Leu	Leu	Leu	Lys	Tyr	Arg	Gln	Gly	Arg	Thr	Ile	Ile	Leu	Ser	Thr
			1075				1080					1085			
His	His	Met	Asp	Glu	Ala	Asp	Val	Leu	Gly	Asp	Arg	Ile	Ala	Ile	Ile
		1090				1095					1100				
Ser	His	Gly	Lys	Leu	Cys	Cys	Val	Gly	Ser	Ser	Leu	Phe	Leu	Lys	Asn
1105					1110						1115				1120
Gln	Leu	Gly	Thr	Gly	Tyr	Tyr	Leu	Thr	Leu	Val	Lys	Lys	Asp	Val	Glu
				1125					1130					1135	
Ser	Ser	Leu	Ser	Ser	Cys	Arg	Asn	Ser	Ser	Ser	Thr	Val	Ser	Tyr	Leu
			1140					1145					1150		
Lys	Lys	Glu	Asp	Ser	Val	Ser	Gln	Ser	Ser	Ser	Asp	Ala	Gly	Leu	Gly
		1155					1160				1165				
Ser	Asp	His	Glu	Ser	Asp	Thr	Leu	Thr	Ile	Asp	Val	Ser	Ala	Ile	Ser
		1170				1175					1180				
Asn	Leu	Ile	Arg	Lys	His	Val	Ser	Glu	Ala	Arg	Leu	Val	Glu	Asp	Ile
1185					1190					1195					1200
Gly	His	Glu	Leu	Thr	Tyr	Val	Leu	Pro	Tyr	Glu	Ala	Ala	Lys	Glu	Gly
				1205					1210					1215	

Ala Phe Val Glu Leu Phe His Glu Ile Asp Asp Arg Leu Ser Asp Leu
 1220 1225 1230
 Gly Ile Ser Ser Tyr Gly Ile Ser Glu Thr Thr Leu Glu Ile Phe
 1235 1240 1245
 Leu Lys Val Ala Glu Glu Ser Gly Val Asp Ala Glu Thr Ser Asp Gly
 1250 1255 1260
 Thr Leu Pro Ala Arg Arg Asn Arg Arg Ala Phe Gly Asp Lys Gln Ser
 1265 1270 1275 1280
 Cys Leu Arg Pro Phe Thr Glu Asp Asp Ala Ala Asp Pro Asn Asp Ser
 1285 1290 1295
 Asp Ile Asp Pro Glu Ser Arg Glu Thr Asp Leu Leu Ser Gly Met Asp
 1300 1305 1310
 Gly Lys Gly Ser Tyr Gln Val Lys Gly Trp Lys Leu Thr Gln Gln Gln
 1315 1320 1325
 Phe Val Ala Leu Leu Trp Lys Arg Leu Leu Ile Ala Arg Arg Ser Arg
 1330 1335 1340
 Lys Gly Phe Phe Ala Gln Ile Val Leu Pro Ala Val Phe Val Cys Ile
 1345 1350 1355 1360
 Ala Leu Val Phe Ser Leu Ile Val Pro Pro Phe Gly Lys Tyr Pro Ser
 1365 1370 1375
 Leu Glu Leu Gln Pro Trp Met Tyr Asn Glu Gln Tyr Thr Phe Val Ser
 1380 1385 1390
 Asn Asp Ala Pro Glu Asp Thr Gly Thr Leu Glu Leu Leu Asn Ala Leu
 1395 1400 1405
 Thr Lys Asp Pro Gly Phe Gly Thr Arg Cys Met Glu Gly Asn Pro Ile
 1410 1415 1420
 Pro Asp Thr Pro Cys Gln Ala Gly Glu Glu Glu Trp Thr Thr Ala Pro
 1425 1430 1435 1440
 Val Pro Gln Thr Ile Met Asp Leu Phe Gln Asn Gly Asn Trp Thr Met
 1445 1450 1455
 Gln Asn Pro Ser Pro Ala Cys Gln Cys Ser Ser Asp Lys Ile Lys Lys
 1460 1465 1470
 Met Leu Pro Val Cys Pro Pro Gly Ala Gly Gly Leu Pro Pro Pro Gln
 1475 1480 1485
 Arg Lys Gln Asn Thr Ala Asp Ile Leu Gln Asp Leu Thr Gly Arg Asn
 1490 1495 1500
 Ile Ser Asp Tyr Leu Val Lys Thr Tyr Val Gln Ile Ile Ala Lys Ser
 1505 1510 1515 1520
 Leu Lys Asn Lys Ile Trp Val Asn Glu Phe Arg Tyr Gly Gly Phe Ser
 1525 1530 1535
 Leu Gly Val Ser Asn Thr Gln Ala Leu Pro Pro Ser Gln Glu Val Asn
 1540 1545 1550
 Asp Ala Ile Lys Gln Met Lys Lys His Leu Lys Leu Ala Lys Asp Ser
 1555 1560 1565
 Ser Ala Asp Arg Phe Leu Asn Ser Leu Gly Arg Phe Met Thr Gly Leu
 1570 1575 1580
 Asp Thr Arg Asn Asn Val Lys Val Trp Phe Asn Asn Lys Gly Trp His
 1585 1590 1595 1600
 Ala Ile Ser Ser Phe Leu Asn Val Ile Asn Asn Ala Ile Leu Arg Ala
 1605 1610 1615
 Asn Leu Gln Lys Gly Glu Asn Pro Ser His Tyr Gly Ile Thr Ala Phe
 1620 1625 1630
 Asn His Pro Leu Asn Leu Thr Lys Gln Gln Leu Ser Glu Val Ala Leu
 1635 1640 1645

Met Thr Thr Ser Val Asp Val Leu Val Ser Ile Cys Val Ile Phe Ala
 1650 1655 1660
 Met Ser Phe Val Pro Ala Ser Phe Val Val Phe Leu Ile Gln Glu Arg
 1665 1670 1675 1680
 Val Ser Lys Ala Lys His Leu Gln Phe Ile Ser Gly Val Lys Pro Val
 1685 1690 1695
 Ile Tyr Trp Leu Ser Asn Phe Val Trp Asp Met Cys Asn Tyr Val Val
 1700 1705 1710
 Pro Ala Thr Leu Val Ile Ile Phe Ile Cys Phe Gln Gln Lys Ser
 1715 1720 1725
 Tyr Val Ser Ser Thr Asn Leu Pro Val Leu Ala Leu Leu Leu Leu
 1730 1735 1740
 Tyr Gly Trp Ser Ile Thr Pro Leu Met Tyr Pro Ala Ser Phe Val Phe
 1745 1750 1755 1760
 Lys Ile Pro Ser Thr Ala Tyr Val Val Leu Thr Ser Val Asn Leu Phe
 1765 1770 1775
 Ile Gly Ile Asn Gly Ser Val Ala Thr Phe Val Leu Glu Leu Phe Thr
 1780 1785 1790
 Asp Asn Lys Leu Asn Asn Ile Asn Asp Ile Leu Lys Ser Val Phe Leu
 1795 1800 1805
 Ile Phe Pro His Phe Cys Leu Gly Arg Gly Leu Ile Asp Met Val Lys
 1810 1815 1820
 Asn Gln Ala Met Ala Asp Ala Leu Glu Arg Phe Gly Glu Asn Arg Phe
 1825 1830 1835 1840
 Val Ser Pro Leu Ser Trp Asp Leu Val Gly Arg Asn Leu Phe Ala Met
 1845 1850 1855
 Ala Val Glu Gly Val Val Phe Phe Leu Ile Thr Val Leu Ile Gln Tyr
 1860 1865 1870
 Arg Phe Phe Ile Arg Pro Arg Pro Val Asn Ala Lys Leu Ser Pro Leu
 1875 1880 1885
 Asn Asp Glu Asp Glu Asp Val Arg Arg Glu Arg Gln Arg Ile Leu Asp
 1890 1895 1900
 Gly Gly Gly Gln Asn Asp Ile Leu Glu Ile Lys Glu Leu Thr Lys Ile
 1905 1910 1915 1920
 Tyr Arg Arg Lys Arg Lys Pro Ala Val Asp Arg Ile Cys Val Gly Ile
 1925 1930 1935
 Pro Pro Gly Glu Cys Phe Gly Leu Leu Gly Val Asn Gly Ala Gly Lys
 1940 1945 1950
 Ser Ser Thr Phe Lys Met Leu Thr Gly Asp Thr Thr Val Thr Arg Gly
 1955 1960 1965
 Asp Ala Phe Leu Asn Lys Asn Ser Ile Leu Ser Asn Ile His Glu Val
 1970 1975 1980
 His Gln Asn Met Gly Tyr Cys Pro Gln Phe Asp Ala Ile Thr Glu Leu
 1985 1990 1995 2000
 Leu Thr Gly Arg Glu His Val Glu Phe Phe Ala Leu Leu Arg Gly Val
 2005 2010 2015
 Pro Glu Lys Glu Val Gly Lys Val Gly Glu Trp Ala Ile Arg Lys Leu
 2020 2025 2030
 Gly Leu Val Lys Tyr Gly Glu Lys Tyr Ala Gly Asn Tyr Ser Gly Gly
 2035 2040 2045
 Asn Lys Arg Lys Leu Ser Thr Ala Met Ala Leu Ile Gly Gly Pro Pro
 2050 2055 2060
 Val Val Phe Leu Asp Glu Pro Thr Thr Gly Met Asp Pro Lys Ala Arg
 2065 2070 2075 2080

Arg Phe Leu Trp Asn Cys Ala Leu Ser Val Val Lys Glu Gly Arg Ser
 2085 2090 2095
 Val Val Leu Thr Ser His Ser Met Glu Glu Cys Glu Ala Leu Cys Thr
 2100 2105 2110
 Arg Met Ala Ile Met Val Asn Gly Arg Phe Arg Cys Leu Gly Ser Val
 2115 2120 2125
 Gln His Leu Lys Asn Arg Phe Gly Asp Gly Tyr Thr Ile Val Val Arg
 2130 2135 2140
 Ile Ala Gly Ser Asn Pro Asp Leu Lys Pro Val Gln Asp Phe Phe Gly
 2145 2150 2155 2160
 Leu Ala Phe Pro Gly Ser Val Leu Lys Glu Lys His Arg Asn Met Leu
 2165 2170 2175
 Gln Tyr Gln Leu Pro Ser Ser Leu Ser Ser Leu Ala Arg Ile Phe Ser
 2180 2185 2190
 Ile Leu Ser Gln Ser Lys Lys Arg Leu His Ile Glu Asp Tyr Ser Val
 2195 2200 2205
 Ser Gln Thr Thr Leu Asp Gln Val Phe Val Asn Phe Ala Lys Asp Gln
 2210 2215 2220
 Ser Asp Asp Asp His Leu Lys Asp Leu Ser Leu His Lys Asn Gln Thr
 2225 2230 2235 2240
 Val Val Asp Val Ala Val Leu Thr Ser Phe Leu Gln Asp Glu Lys Val
 2245 2250 2255
 Lys Glu Ser Tyr Val
 2260

<210> 6
 <211> 7860
 <212> DNA
 <213> homo sapien

<400> 6
 gtccctgctg tgagctctgg ccgctgcctt ccagggctcc cgagccacac gctgggggtg 60
 ctggctgagg gaacatgggt tgttgccctc agctgaggtt gctgctgtgg aagaacctca 120
 ctttcagaag aagacaaaca tgtcagctgt tactggaagt ggcttggcct ctatttatct 180
 tcctgatact gatctctgtt cggctgagct acccacccta tgaacaacat gaatgccatt 240
 ttccaaataa agccatgccc tctgcaggaa cacttccttg gggtcagggg attatctgta 300
 atgccaacaa cccctgtttc cgttaccgga ctccctggga ggctcccgga gttgttggaa 360
 actttaacaa atccattgtg gctcgctgtt tctcagatgc tcggaggctt cttttataca 420
 gccagaaaga caccagcatg aaggacatgc gcaaagtctt gagaacatta cagcagatca 480
 agaaatccag ctcaaacttg aagcttcaag atttcttggt ggacaatgaa accttctctg 540
 gggttcctgta tcacaacctc tctctcccaa agtctactgt ggacaagatg ctgagggtcg 600
 atgtcattct ccacaaggta tttttgcaag gctaccagtt acatttgaca agtctgtgca 660
 atggatcaaa atcagaagag atgattcaac ttggtgacca agaagtttct gagctttgtg 720
 gcctaccaag ggagaaactg gctgcagcag agcaggtact tcgttccaac atggacatcc 780
 tgaagccaat cctgagaaca ctaaactcta catctccctt cccgagcaag gagctggctg 840
 aagccacaaa aacattgctg catagtcttg ggactctggc ccaggagctg ttcagcatga 900
 gaagctggag tgacatgcga caggaggtga tgtttctgac caatgtgaac agctccagct 960
 cctccaccca aatctaccag gctgtgtctc gtattgtctg cgggcatccc gagggagggg 1020
 ggctgaagat caagtctctc aactggtatg aggacaacaa ctacaaagcc ctctttggag 1080
 gcaatggcac tgaggaagat gctgaaacct tctatgacaa ctctacaact ccttactgca 1140
 atgatttgat gaagaatttg gagtctagtc ctctttcccg cattatcttg aaagctctga 1200
 agccgctgct cgttgggaag atcctgtata cacctgacac tccagccaca aggcaggtca 1260
 tggctgaggt gaacaagacc ttccaggaac tggctgtgtt ccatgatctg gaaggcatgt 1320

```

gggaggaact cagccccaag atctggacct tcatggagaa cagccaagaa atggaccttg 1380
tccggatgct gttggacagc agggacaatg accacttttg ggaacagcag ttggatggct 1440
tagattggac agcccaagac atcgtggcgt ttttggccaa gcaccagag gatgtccagt 1500
ccagtaatgg ttctgtgtac acctggagag aagctttcaa cgagactaac caggcaatcc 1560
ggaccatata tcgcttcata gagtgtgtca acctgaacaa gctagaaccc atagcaacag 1620
aagtctggct catcaacaag tccatggagc tgctggatga gaggaagttc tgggctggta 1680
ttgtgttcac tgggaattact ccaggcagca ttgagctgcc ccatcatgtc aagtacaaga 1740
tccgaatgga cattgacaat gtggagagga caaataaaat caaggatggg tactggggacc 1800
ctggtccctc agctgacccc tttaggagca tgcggtacgt ctgggggggc ttgcctact 1860
tgcaggatgt ggtggagcag gcaatcatca ttgagctgac gggcaccgag aagaaaactg 1920
gtgtctatat gcaacagatg cccatccctt gttacgttga tgacatcttt ctgcggtgta 1980
tgagccgggtc aatgcccttc ttcatacgc tggcctggat ttactcagt gctgtgatca 2040
tcaagggcat cgtgtatgag aaggaggcac ggctgaaaga gaccatgcgg atcatggggc 2100
tggacaacag catcctctgg tttagctggt ccatctcct cctcttctga 2160
gcgctggcct gctagtggct atcctgaagt taggaaacct gctgccctac agtgatecca 2220
gcgtgggtgt tgtcttctcg tccgtgtttg ctgtggtgac aatcctgcag tgcttccctga 2280
ttagcacact cttctccaga gccaaacctg cagcagcctg tggggggcatc atctacttca 2340
cgctgtacct gccctacgtc ctgtgtgttg catggcagga ctacgtgggc ttcacactca 2400
agatcttcgc tagcctgctg tctcctgttg cttttgggtt tggctgtgag tactttggcc 2460
tttttgagga gcagggcatt ggagtgcagt gggacaacct gtttgagagt cctgtggagg 2520
aagatggctt caatctcacc acttcgggtc ccatgatgct gtttgacacc ttcctctatg 2580
gggtgatgac ctggtacatt gaggtgtctt ttccaggcca gtacggaatt cccaggccct 2640
ggtatttttc ttgaccaag tctactggt ctgagatgag aagtgatgag aagagccacc 2700
ctggttccaa ccagaagaga atatcagaaa tctgcatgga ggaggaaccc acccacttga 2760
agctggcggt gtccattcag aacctggtaa aagtctaccg agatgggatg aaggtggctg 2820
tcgatggcct ggcaactgaat ttttatgagg gccagatcac ctcttccctg ggccacaatg 2880
gagcggggaa gacgaccacc atgtcaatcc tgaccgggtt gtccccccg acctcgggca 2940
ccgctacat cctgggaaaa gacattcgct ctgagatgag caccatccgg cagaacctgg 3000
gggtctgtcc ccagcataac gtgctgtttg acatgctgac tgtcgaagaa cacatctggt 3060
tctatgcccg cttgaaagggt ctctctgaga agcacgtgaa ggcggagatg gagcagatgg 3120
ccctggatgt tggtttgcca tcaagcaagc tgaaaagcaa acaagccag ctgtcagggtg 3180
gaatgcagag aaagctatct gtggccttgg cctttgtcgg gggatctaag gttgtcattc 3240
tggatgaaac cacagctggt tgggacctt actccgcag gggaaatatg gagctgctgc 3300
tgaataaccg acaaggccgc accattatcc tctctacaca ccacatggat gaagcggacg 3360
tcctggggga caggattgcc atcatctccc atgggaagct gtgctgtgtg ggctcctccc 3420
tgtttctgaa gaaccagctg ggaacaggct actacctgac cttggtcaag aaagatgtgg 3480
aatcctccct cagttccctg agaaacagta gtagcactgt gtcataacct aaaaaggagg 3540
acagtgtttc tcagagcagt tctgatgctg gcctgggcag cgaccatgag agtgacacgc 3600
tgaccatcga tgtctctgct atctccaacc tcatcaggaa gcatgtgtct gaagcccggc 3660
tggtggaaga catagggcat gagctgacct atgtgctgcc atatgaagct gctaaggagg 3720
gagcctttgt ggaactcttt catgagattg atgaccggct ctcagacctg ggcatttcta 3780
gttatggcat ctcagagacg accctggaag aaatatcct caagggtggc gaagagagtg 3840
gggtggatgc tgagacctca gatggtacct tgccagcaag acgaaacagg cgggccttcg 3900
gggacaagca gagctgtctt cgcccgttca ctgaagatga tgctgctgat ccaaattgatt 3960
ctgacataga ccagaaatcc agagagacag acttgctcag tgggatggat ggcaaagggt 4020
cctaccagggt gaaaggctgg aaacttacac gccaacagtt tgtggccctt ttgtggaaga 4080
gactgctaata tgccagacgg agtcggaaag gattttttgc tcagattgtc ttgccagctg 4140
tgtttgtctg cattgccctt gtgttcagcc tgatcgtgcc accctttggc aagtaccca 4200
gcctggaaact tcagccctgg atgtacaacg aacagtacac atttgtcagc aatgatgctc 4260
ctgaggacac gggaaacctg gaactcttaa acgccctcac caaagacctt ggcttcggga 4320
cccgtgtat ggaaggaaac ccaatcccag acacgccctg ccaggcaggg gaggaagagt 4380
ggaccactgc cccagttccc cagaccatca tggacctctt ccagaatggg aactggacaa 4440
tgcagaaccc ttcacctgca tgccagtgtg gcagcgacaa aatcaagaag atgctgctg 4500
tgtgtccccc aggggcagggt gggctgcctc ctccacaaag aaaacaaaac actgcagata 4560

```

tccttcagga	cctgacagga	agaaacattt	cggattatct	ggtgaagacg	tatgtgcaga	4620
tcatagccaa	aagcttaaag	aacaagatct	gggtgaatga	gtttaggtat	ggcggctttt	4680
ccctgggtgt	cagtaatact	caagcacttc	ctccgagtca	agaagttaat	gatgccatca	4740
aacaaatgaa	gaaacaccta	aagctggcca	aggacagttc	tgcagatcga	tttctcaaca	4800
gcttgggaag	atztatgaca	ggactggaca	ccagaaataa	tgtcaagggtg	tggttcaata	4860
acaagggctg	gcatgcaatc	agctctttcc	tgaatgtcat	caacaatgcc	attctccggg	4920
ccaacctgca	aaagggagag	aaccctagcc	attatggaat	tactgctttc	aatcatcccc	4980
tgaatctcac	caagcagcag	ctctcagagg	tggctctgat	gaccacatca	gtggatgtcc	5040
ttgtgtccat	ctgtgtcatc	tttgcaatgt	ccttcgtccc	agccagcttt	gtcgtattcc	5100
tgatccagga	gcgggtcagc	aaagcaaaac	acctgcagtt	catcagtggg	gtgaagcctg	5160
tcattctactg	gctctctaata	tttgtctggg	atatgtgcaa	ttacgttgtc	cctgccacac	5220
tggtcattat	catcttcac	tgcttcacgc	agaagtccca	tgtgtcctcc	accaatctgc	5280
ctgtgctagc	ccttctactt	ttgctgtatg	gggtgtcaat	cacacctctc	atgtacccag	5340
cctcctttgt	gttcaagatc	cccagcacag	cttatgtggt	gctcaccagc	gtgaacctct	5400
tcattggcat	taatggcagc	gtggccacct	ttgtgctgga	gctgttcacc	gacaataaagc	5460
tgaataatat	caatgatata	ctgaagtccg	tgttcttgat	cttcccacat	ttttgcctgg	5520
gacgagggct	catcgacatg	gtgaaaaaac	aggcaatggc	tgatgccctg	gaaaggtttg	5580
gggagaatcg	ctttgtgtca	ccattatctt	gggacttggt	gggacgaaac	ctcttcgcga	5640
tggtccgtga	aggggtgggtg	ttcttctcca	ttactgttct	gatccagtag	agattcttca	5700
tcaggccccag	acctgtaaat	gcaaagctat	ctcctctgaa	tgatgaagat	gaagatgtga	5760
ggcgggaaag	acagagaatt	cttgatgggtg	gaggccagaa	tgacatctta	gaaatcaagg	5820
agttgacgaa	gatataataga	aggaagcgga	agcctgctgt	tgacaggatt	tgctgtgggca	5880
ttcttcctgg	tgagtgcctt	gggtcctctg	gagttaatgg	ggctggaaaa	tcatacaact	5940
tcaagatggt	aacaggagat	accactgtta	ccagaggaga	tgctttcctt	aacaaaaata	6000
gtatcttata	aaacatccat	gaagtacatc	agaacatggg	ctactgccct	cagtttgatg	6060
ccatcacaga	gctgttgact	gggagagaa	acgtggagtt	ctttgccctt	ttgagaggag	6120
ttccagagaa	agaagttggc	aaggttggtg	agtgggcgat	tcggaaactg	ggcctcgtga	6180
agttgggaga	aaaatatgct	ggtaactata	gtggaggcaa	caaacgcaag	ctctctacag	6240
ccatggcttt	gatcggcggg	cctcctgtgg	tgtttctgga	tgaaccacc	acaggcatgg	6300
atcccaaaagc	ccggcggttc	ttgtggaatt	gtgccctaag	tgttgtcaag	gaggggagat	6360
cagtgtgct	tacatctcat	agtatggaag	aatgtgaagc	tctttgcact	aggatggcaa	6420
tcattggtcaa	tggaagggtc	aggtgccttg	gcagtgtcca	gcattcaaaa	aataggtttg	6480
gagatgggtta	tacaatagtt	gtacgaatag	cagggtccaa	cccgacctg	aagcctgtcc	6540
aggattttct	tggaacttgca	tttctctgga	gtgttctaaa	agagaaacac	cggaaacatgc	6600
tacaatacca	gcttccatct	tcattatctt	ctctggccag	gatattcagc	atcctctccc	6660
agagcaaaaa	gcgactccac	atagaagact	actctgtttc	tcagacaaca	cttgaccaag	6720
tatttgtgaa	ctttgccaa	gaccaaagt	atgatgacca	cttaaaagac	ctctcattac	6780
acaaaaacca	gacagtagtg	gacgttgacg	ttctcacatc	ttttctacag	gatgagaaag	6840
tgaagaaag	ctatgtatga	agaatcctgt	tcatacgggg	tggtgaaag	taaagaggaa	6900
ctagactttc	ctttgcacca	tgtgaagtgt	tggtggagaaa	agagccagaa	gttgatgtgg	6960
gaagaagtaa	actggatact	gtactgatac	tattcaatgc	aatgcaattc	aatgcaatga	7020
aaacaaaatt	ccattacagg	ggcagtgctt	ttgtagccta	tgtcttgat	ggctctcaag	7080
tgaagactt	gaatttagtt	ttttacctat	acctatgtga	aactctatta	tggaacccaa	7140
tggaacatag	ggtttgaa	cacacttttt	tttttttttt	tgttctctgtg	tattctcatt	7200
gggttgcaa	caataattca	tcaagtaatc	atggccagcg	attattgatc	aaaatcaaaa	7260
ggtaatgcac	atcctcattc	actaagccat	gccatgcccc	ggagactggg	ttcccggtga	7320
cacatccatt	gctggcaatg	agtgtgccag	agttattagt	gccaagtttt	tcagaaagtt	7380
tgaagcacca	tggtgtgtca	tgctcacttt	tggtgaaagct	gctctgctca	gagtcctatca	7440
acattgaata	tcagttgaca	gaatgggtgc	atgcgtggct	aacatcctgc	tttgattccc	7500
tctgataagc	tgttctgggtg	gcagtaacat	gcaacaaaaa	tgtgggtgtc	tccaggcacg	7560
ggaaacttgg	ttccattggt	atattgtcct	atgcttcgag	ccatgggtct	acagggctcat	7620
ccttatgaga	ctcttaata	tacttagatc	ctggtaagag	gcaaagaatc	aacagccaaa	7680
ctgctggggc	tgcaactgct	gaagccaggg	catgggatta	aagagattgt	gcgttcaaac	7740
ctagggaagc	ctgtgcccac	ttgtcctgac	tgtctgctaa	catggtacac	tgcatctcaa	7800

gatgtttatc tgacacaagt gtattatttc tggctttttg aattaatcta gaaaatgaaa 7860

<210> 7
<211> 16
<212> DNA
<213> homo sapien

<220>
<221> variation
<222> (7)...(11)
<223> N at positions 7-11 is A,T,C, or G

<400> 7
aggtcannnn aggtca 16

<210> 8
<211> 26
<212> DNA
<213> homo sapien

<400> 8
agaggcaggt ggatcatttg aggtca 26

<210> 9
<211> 26
<212> DNA
<213> homo sapien

<400> 9
ttgaggcggg tgatcacttg aggtca 26

<210> 10
<211> 26
<212> DNA
<213> homo sapiens

<400> 10
caaggcgggc agatcacttg aggtta 26

<210> 11
<211> 26
<212> DNA
<213> Homo sapien

<400> 11
caaggtgggc agctcacctc aggtca 26

<210> 12
<211> 24
<212> DNA
<213> Homo sapiens

<220>

<221> variation

<222> (1)...(18)

<223> N at positions 1-6,8,9, and 17 is A,T,C, or G. N
at position 18 is A,T,C, G, or other, including no
nucleotide.

<400> 12

nnnnnnannt tgacctnntg acct

24

<210> 13

<211> 24

<212> DNA

<213> Homo sapiens

<400> 13

ctttgaagcc tgatcatatg acct

24

<210> 14

<211> 24

<212> DNA

<213> Homo sapiens

<400> 14

aggctggtct cgaactcctg acct

24

<210> 15

<211> 24

<212> DNA

<213> Homo sapien

<400> 15

cttaattggt ggwgctgttg acct

24

<210> 16

<211> 24

<212> DNA

<213> Homo sapien

<400> 16

caggatggcg taaactcctg acct

24

<210> 17

<211> 24

<212> DNA

<213> homo sapien

<400> 17

aggttggttt cgaactcctg acct

24

<210> 18

<211> 24

<212> DNA

<213> Homo sapein

<400> 18 tcaaggtagg agaccttggtg gcct	24
<210> 19 <211> 10 <212> DNA <213> homo sapien	
<400> 19 atcacccac	10
<210> 20 <211> 20 <212> DNA <213> homo sapien	
<400> 20 gagatgtgct atgacccac	20
<210> 21 <211> 20 <212> DNA <213> homo sapien	
<400> 21 gtgagcccag atcacaccac	20
<210> 22 <211> 20 <212> DNA <213> homo sapien	
<400> 22 tccatccatc cacacccac	20
<210> 23 <211> 20 <212> DNA <213> homo sapien	
<400> 23 cccttttatt aacacctcac	20
<210> 24 <211> 20 <212> DNA <213> homo sapien	
<400> 24 gtaagccaag atcatgccac	20

<210> 25
<211> 20
<212> DNA
<213> homo sapien

<400> 25
acctcaagtg atcacccgcc 20

<210> 26
<211> 20
<212> DNA
<213> homo sapien

<400> 26
ggctcaagcg atcctcccac 20

<210> 27
<211> 20
<212> DNA
<213> homo sapien

<400> 27
ccatgattgg atcactgcac 20

<210> 28
<211> 20
<212> DNA
<213> homo sapien

<400> 28
gtgagtcgag atcatgccac 20

<210> 29
<211> 20
<212> DNA
<213> homo sapien

<400> 29
tgcttttggt ttccccccac 20

<210> 30
<211> 20
<212> DNA
<213> homo sapien

<400> 30
ccgccttccc ctcaccccag 20

<210> 31
<211> 20
<212> DNA
<213> homo sapien

<400> 31
accctccacc cccacccac 20

<210> 32
<211> 16
<212> DNA
<213> homo sapien

<220>
<221> variation
<222> (1)...(11)
<223> N at positions 2-9 is A,T,C, or G. N at positions
1 and 10 is A or T. N at position 11 is A or G.

<400> 32
nnnnnnnnnn nggtca 16

<210> 33
<211> 18
<212> DNA
<213> homo sapien

<400> 33
ctgggcaagg atgggtca 18

<210> 34
<211> 17
<212> DNA
<213> homo sapiens

<400> 34
tgggcaagga tgggtca 17

<210> 35
<211> 17
<212> DNA
<213> homo sapiens

<400> 35
aaaaagcacc aaggtca 17

<210> 36
<211> 17
<212> DNA
<213> homo sapien

<400> 36
agaagatgcc aggggtca 17

<210> 37
<211> 17
<212> DNA
<213> homo sapiens

<400> 37	
gaggagatgg aggggtca	17
<210> 38	
<211> 26	
<212> DNA	
<213> homo sapiens	
<400> 38	
ccgagcgcag aggttactat cgggtca	26
<210> 39	
<211> 26	
<212> DNA	
<213> homo sapien	
<400> 39	
gcccaattccc aggtcagaac agacca	26
<210> 40	
<211> 20	
<212> DNA	
<213> homo sapien	
<400> 40	
ggacctgcag ctctccccac	20
<210> 41	
<211> 17	
<212> DNA	
<213> homo sapien	
<400> 41	
aacgccaag taagtca	17
<210> 42	
<211> 17	
<212> DNA	
<213> homo sapien	
<400> 42	
gagctcgtac taggaca	17
<210> 43	
<211> 17	
<212> DNA	
<213> homo sapien	
<400> 43	
gcagagtcct ggggtca	17
<210> 44	
<211> 18	
<212> DNA	

<213> homo sapien

<400> 44
cgcagagtcc tgggggtca 18

<210> 45
<211> 17
<212> DNA
<213> homo sapien

<400> 45
agccaattcc cagggtca 17

<210> 46
<211> 17
<212> DNA
<213> homo sapien

<400> 46
acggaccggt tgggaca 17

<210> 47
<211> 18
<212> DNA
<213> homo sapien

<400> 47
cacggaccgt ttgggaca 18

<210> 48
<211> 19
<212> DNA
<213> homo sapien

<400> 48
ccacggaccg tttgggaca 19

<210> 49
<211> 18
<212> DNA
<213> homo sapien

<400> 49
actagaggcc ttgggtct 18

<210> 50
<211> 17
<212> DNA
<213> homo sapien

<400> 50
ctagaggcct tgggtct 17

<210> 51

<211> 17
<212> DNA
<213> homo sapien

<400> 51
ccctaccct caggta 17

<210> 52
<211> 18
<212> DNA
<213> homo sapien

<400> 52
tccctacccc tcaggta 18

<210> 53
<211> 17
<212> DNA
<213> homo sapien

<220>
<221> variation
<222> (2)...(2)
<223> N at position 2 is C or G.

<400> 53
gntctgcgcc agggaca 17

<210> 54
<211> 17
<212> DNA
<213> homo sapien

<220>
<221> variation
<222> (12)...(12)
<223> N at position 12 is A,T,C, or G.

<400> 54
ttttagttag anggtta 17

<210> 55
<211> 26
<212> DNA
<213> homo sapien

<400> 55
tgaggcaggt agatcacttg aggtca 26

<210> 56
<211> 26
<212> DNA
<213> homo sapien

<400> 56
cgaggctggc ggatcacctg aggtca 26

<210> 57
<211> 26
<212> DNA
<213> homo sapien

<400> 57
aagcctaaca aggttactga aggcca 26

<210> 58
<211> 26
<212> DNA
<213> homo sapien

<400> 58
agaggtgggc ggatcacctg aggtca 26

<210> 59
<211> 24
<212> DNA
<213> homo sapien

<400> 59
ctcgatttcc tgacctcgtg atcc 24

<210> 60
<211> 24
<212> DNA
<213> homo sapien

<400> 60
caaaacattg tgcccttttg aact 24

<210> 61
<211> 24
<212> DNA
<213> homo sapien

<400> 61
gcgctagggt tgcctcatt acct 24

<210> 62
<211> 24
<212> DNA
<213> homo sapien

<400> 62
ctcgatttct tgacctcgtg atcc 24

<210> 63
<211> 20
<212> DNA

<213> homo sapien

<400> 63

gtgagctgag atcacaccac

20

<210> 64

<211> 20

<212> DNA

<213> homo sapien

<400> 64

ttcaaggatg atcaccacat

20

<210> 65

<211> 20

<212> DNA

<213> homo sapien

<400> 65

ggctcaagtg atcctccac

20

<210> 66

<211> 20

<212> DNA

<213> homo sapien

<400> 66

gtgagccgag atcgcgccac

20

<210> 67

<211> 20

<212> DNA

<213> homo sapien

<400> 67

gtgagttatg atcatgccac

20

<210> 68

<211> 20

<212> DNA

<213> homo sapien

<400> 68

ccactgtttg aacaaccac

20

<210> 69

<211> 20

<212> DNA

<213> homo sapien

<400> 69

acctcaggtg atccgcccac

20

<210> 70

<211> 20
<212> DNA
<213> homo sapien

<400> 70
aaatgtgaca atctccacac

20

<210> 71
<211> 20
<212> DNA
<213> homo sapien

<400> 71
aatatagaat atcacctccc

20

<210> 72
<211> 20
<212> DNA
<213> homo sapien

<400> 72
ccttttatct accaccaac

20

<210> 73
<211> 17
<212> DNA
<213> homo sapien

<400> 73
ccttggtgga tgggtca

17

<210> 74
<211> 18
<212> DNA
<213> homo sapien

<400> 74
gccttggttg atgggtca

18

<210> 75
<211> 17
<212> DNA
<213> homo sapien

<400> 75
ttgctgtgag tgggtca

17

<210> 76
<211> 17
<212> DNA
<213> homo sapien

<400> 76
gccttcgaga aggggtca

17

<210> 77
<211> 18
<212> DNA
<213> homo sapien

<400> 77
ggccttgacag aagggtca

18

<210> 78
<211> 18
<212> DNA
<213> homo sapien

<400> 78
aattaagctg atgggtca

18

<210> 79
<211> 17
<212> DNA
<213> homo sapien

<400> 79
attaagctga tgggtca

17

<210> 80
<211> 18
<212> DNA
<213> homo sapien

<400> 80
aggtgctaac taggtca

18

<210> 81
<211> 17
<212> DNA
<213> homo sapien

<400> 81
ggtgctaact aggtca

17

<210> 82
<211> 17
<212> DNA
<213> homo sapien

<400> 82
atgggatgac tgggtca

17

<210> 83
<211> 17
<212> DNA
<213> homo sapien

<400> 83

tctccatgcc aagggtca	17
<210> 84	
<211> 23	
<212> DNA	
<213> homo sapien	
<400> 84	
ttgaggacat gcggtacgtc tgg	23
<210> 85	
<211> 23	
<212> DNA	
<213> homo sapien	
<400> 85	
ttgaggacat gtggtacgtc tgg	23
<210> 86	
<211> 21	
<212> DNA	
<213> homo sapien	
<400> 86	
gcctacttgc aggatgtggt g	21
<210> 87	
<211> 21	
<212> DNA	
<213> homo sapien	
<400> 87	
gcctacttgc gggatgtggt g	21
<210> 88	
<211> 23	
<212> DNA	
<213> homo sapien	
<400> 88	
cctcattcct cttcttgtga gcg	23
<210> 89	
<211> 20	
<212> DNA	
<213> homo sapien	
<400> 89	
cctcattcct cttgtgagcg	20
<210> 90	
<211> 21	
<212> DNA	
<213> homo sapien	

<400> 90
aaaagtctac cgagatggga t 21

<210> 91
<211> 21
<212> DNA
<213> homo sapien

<400> 91
aaaagtctac tgagatggga t 21

<210> 92
<211> 21
<212> DNA
<213> homo sapien

<400> 92
ggccagatca cctccttcct g 21

<210> 93
<211> 21
<212> DNA
<213> homo sapien

<400> 93
ggccagatca tctccttcct g 21

<210> 94
<211> 21
<212> DNA
<213> homo sapien

<400> 94
acacaccaca tggatgaagc g 21

<210> 95
<211> 21
<212> DNA
<213> homo sapien

<400> 95
acacaccaca cggatgaagc g 21

<210> 96
<211> 21
<212> DNA
<213> homo sapien

<400> 96
cctggaagaa gtaagttaag t 21

<210> 97
<211> 21
<212> DNA

<213> homo sapien

<400> 97
cctggaagaa ctaagttaag t 21

<210> 98
<211> 21
<212> DNA
<213> homo sapien

<400> 98
gctgcctgtg tgcctcccag g 21

<210> 99
<211> 21
<212> DNA
<213> homo sapien

<400> 99
gctgcctgtg cgtccccag g 21

<210> 100
<211> 22
<212> DNA
<213> homo sapien

<400> 100
tagccattat ggaattactg ct 22

<210> 101
<211> 21
<212> DNA
<213> homo sapien

<400> 101
tagccattat caattactgc t 21

<210> 102
<211> 26
<212> DNA
<213> homo sapien

<400> 102
gatgaagatg aagatgtgag gcggga 26

<210> 103
<211> 20
<212> DNA
<213> homo sapien

<400> 103
gatgaagatg tgaggcggga 20

<210> 104

<211> 21
<212> DNA
<213> homo sapien

<400> 104
aatagttgta cgaatagcag g 21

<210> 105
<211> 21
<212> DNA
<213> homo sapien

<400> 105
aatagttgta tgaatagcag g 21

<210> 106
<211> 20
<212> DNA
<213> homo sapien

<400> 106
atagttgtac gaatagcagg 20

<210> 107
<211> 19
<212> DNA
<213> homo sapien

<400> 107
atagttgtag aatagcagg 19

<210> 108
<211> 20
<212> DNA
<213> homo sapien

<400> 108
gggtccaacc cggacctgaa 20

<210> 109
<211> 20
<212> DNA
<213> homo sapien

<400> 109
gggtccaacc tggacctgaa 20

<210> 110
<211> 21
<212> DNA
<213> homo sapien

<400> 110
cattatcttc tctggccagg a 21

<210> 111
<211> 20
<212> DNA
<213> homo sapien

<400> 111
cattatcttt ttggccagga 20

<210> 112
<211> 20
<212> DNA
<213> homo sapien

<400> 112
ggaactagtc ccggcaaaaa 20

<210> 113
<211> 20
<212> DNA
<213> homo sapien

<400> 113
ggaactagtc tcggcaaaaa 20

<210> 114
<211> 17
<212> DNA
<213> homo sapien

<400> 114
ccgggacccg cagagcc 17

<210> 115
<211> 17
<212> DNA
<213> homo sapien

<400> 115
ccgggaccgg cagagcc 17

<210> 116
<211> 20
<212> DNA
<213> homo sapien

<400> 116
accagccacg gcgtccctgc 20

<210> 117
<211> 21
<212> DNA
<213> homo sapien

<400> 117

accagccacg ggcgtccctg c 21

<210> 118
<211> 21
<212> DNA
<213> homo sapien

<400> 118
acacgctggg ggtgctggct g 21

<210> 119
<211> 21
<212> DNA
<213> homo sapien

<400> 119
acacgctggg cgtgctggct g 21

<210> 120
<211> 21
<212> DNA
<213> homo sapien

<400> 120
ctgggttcct gtatcacaac c 21

<210> 121
<211> 21
<212> DNA
<213> homo sapien

<400> 121
ctgggttcct atatcacaac c 21

<210> 122
<211> 21
<212> DNA
<213> homo sapien

<400> 122
ggcctaccaa gggagaaact g 21

<210> 123
<211> 21
<212> DNA
<213> homo sapien

<400> 123
ggcctaccaa aggagaaact g 21

<210> 124
<211> 21
<212> DNA
<213> homo sapien

<400> 124
gcggggcatcc cgaggaggagg g 21

<210> 125
<211> 21
<212> DNA
<213> homo sapien

<400> 125
gcggggcatcc tgaggaggagg g 21

<210> 126
<211> 21
<212> DNA
<213> homo sapien

<400> 126
agggaggagg gctgaagatc a 21

<210> 127
<211> 21
<212> DNA
<213> homo sapien

<400> 127
agggaggagg actgaagatc a 21

<210> 128
<211> 21
<212> DNA
<213> homo sapien

<400> 128
tgactccagg tgaacaagac c 21

<210> 129
<211> 21
<212> DNA
<213> homo sapien

<400> 129
tgactccagg cgaacaagac c 21

<210> 130
<211> 21
<212> DNA
<213> homo sapien

<400> 130
gcaggactac gtgggcttca c 21

<210> 131
<211> 21
<212> DNA
<213> homo sapien

<400> 131
gcaggactac atgggcttca c 21

<210> 132
<211> 21
<212> DNA
<213> homo sapien

<400> 132
cgtgggcttc acactcaaga t 21

<210> 133
<211> 21
<212> DNA
<213> homo sapien

<400> 133
cgtgggcttc ccactcaaga t 21

<210> 134
<211> 21
<212> DNA
<213> homo sapien

<400> 134
tcacactcaa gatcttcgct g 21

<210> 135
<211> 21
<212> DNA
<213> homo sapien

<400> 135
tcacactcaa catcttcgct g 21

<210> 136
<211> 17
<212> DNA
<213> homo sapien

<400> 136
ccacttcggt ctccatg 17

<210> 137
<211> 17
<212> DNA
<213> homo sapien

<400> 137 ccacttcgat ctccatg	17
<210> 138 <211> 18 <212> DNA <213> homo sapien	
<400> 138 gaagagaata tcagaaag	18
<210> 139 <211> 18 <212> DNA <213> homo sapien	
<400> 139 gaagagaatg tcagaaag	18
<210> 140 <211> 21 <212> DNA <213> homo sapien	
<400> 140 gatctaaggt tgtcattctg g	21
<210> 141 <211> 21 <212> DNA <213> homo sapien	
<400> 141 gatctaaggt ggtcattctg g	21
<210> 142 <211> 20 <212> DNA <213> homo sapien	
<400> 142 gcgaccatga gagtgacacg	20
<210> 143 <211> 20 <212> DNA <213> homo sapien	
<400> 143 gcgaccatga cagtgacacg	20
<210> 144 <211> 21 <212> DNA	

<213> homo sapien

<400> 144

ctggacacca gaaataatgt c

21

<210> 145

<211> 21

<212> DNA

<213> homo sapien

<400> 145

ctggacacca aaaataatgt c

21

<210> 146

<211> 21

<212> DNA

<213> homo sapien

<400> 146

tcctatgtgt cctccaccaa t

21

<210> 147

<211> 21

<212> DNA

<213> homo sapien

<400> 147

tcctatgtgt gctccaccaa t

21

<210> 148

<211> 21

<212> DNA

<213> homo sapien

<400> 148

caggggtccaa cccggacctg a

21

<210> 149

<211> 21

<212> DNA

<213> homo sapien

<400> 149

caggggtccaa tccggacctg a

21

<210> 150

<211> 22

<212> DNA

<213> homo sapien

<400> 150

cgggggaag gacgcagac cg

22

<210> 151

<211> 22
<212> DNA
<213> homo sapien

<400> 151
cgggggaagg ggacgcagac cg 22

<210> 152
<211> 17
<212> DNA
<213> homo sapien

<400> 152
ggccgggaac ggggcgg 17

<210> 153
<211> 17
<212> DNA
<213> homo sapien

<400> 153
ggccgggaag ggggcgg 17

<210> 154
<211> 21
<212> DNA
<213> homo sapien

<400> 154
agtatccctt gtacacgaga a 21

<210> 155
<211> 25
<212> DNA
<213> homo sapien

<400> 155
agtatccctc ccttggtcac gagaa 25

<210> 156
<211> 21
<212> DNA
<213> homo sapien

<400> 156
gtgacaccca acggagtagg g 21

<210> 157
<211> 21
<212> DNA
<213> homo sapien

<400> 157
gtgacaccca gcggagtagg g 21

<210> 158
<211> 25
<212> DNA
<213> homo sapien

<400> 158
tatgtgctga ccatgggagc ttgtt 25

<210> 159
<211> 25
<212> DNA
<213> homo sapien

<400> 159
tatgtgctga ccgtgggagc ttgtt 25

<210> 160
<211> 25
<212> DNA
<213> homo sapien

<400> 160
cctccgcctg ccaggttcag cgatt 25

<210> 161
<211> 25
<212> DNA
<213> homo sapien

<400> 161
cctccgcctg ccgggttcag cgatt 25

<210> 162
<211> 21
<212> DNA
<213> homo sapien

<400> 162
gaaaattagt atgtaaggaa g 21

<210> 163
<211> 21
<212> DNA
<213> homo sapien

<400> 163
gaaaattagt ctgtaaggaa g 21

<210> 164
<211> 22
<212> DNA
<213> homo sapien

<400> 164
catttttctta gaaaagagag gt 22

<210> 165
<211> 22
<212> DNA
<213> homo sapien

<400> 165
catttttctta gagaagagag gt 22

<210> 166
<211> 20
<212> DNA
<213> homo sapien

<220>
<221> variation
<222> (11)...(11)
<223> N at position 11 is G or T

<400> 166
tttaaaggagg ntgattagga 20

<210> 167
<211> 22
<212> DNA
<213> homo sapien

<220>
<221> variation
<222> (11)...(11)
<223> N at position 11 is G or T

<400> 167
gaagaaattt ntttttttga tt 22

<210> 168
<211> 19
<212> DNA
<213> homo sapien

<400> 168
tctgtcccca tccctgacg 19

<210> 169
<211> 20
<212> DNA
<213> homo sapien

<400> 169
tctgtcccca atccctgacg 20

<210> 170
<211> 20
<212> DNA
<213> homo sapien

<400> 170
aggagccaaa cgctcattgt

20

<210> 171
<211> 21
<212> DNA
<213> homo sapien

<400> 171
aggagccaaa gcgctcattg t

21

<210> 172
<211> 21
<212> DNA
<213> homo sapien

<400> 172
aagccactgt ttttaaccag t

21

<210> 173
<211> 21
<212> DNA
<213> homo sapien

<400> 173
aagccactgt atttaaccag t

21

<210> 174
<211> 22
<212> DNA
<213> homo sapien

<400> 174
gctcccteta gcatgcaggc tc

22

<210> 175
<211> 22
<212> DNA
<213> homo sapien

<400> 175
gctcccteta gtatgcaggc tc

22

<210> 176
<211> 21
<212> DNA
<213> homo sapien

<400> 176
ttgcctgttt ctcacagagc c 21

<210> 177
<211> 19
<212> DNA
<213> homo sapien

<400> 177
ttgcctgttt ctcagagcc 19

<210> 178
<211> 21
<212> DNA
<213> homo sapien

<220>
<221> variation
<222> (10)...(10)
<223> N at position 10 is C or G

<400> 178
gcgcagtgcn ctgtgtcett a 21

<210> 179
<211> 23
<212> DNA
<213> homo sapien

<220>
<221> variation
<222> (12)...(12)
<223> N at position 12 is G or T

<400> 179
ctcttctgtt ancacagaag aga 23

<210> 180
<211> 21
<212> DNA
<213> homo sapien

<220>
<221> variation
<222> (11)...(11)
<223> N at position 11 is A or G

<400> 180
cattctaggg ntcatagcca t 21

<210> 181
<211> 22
<212> DNA

<213> homo sapien

<220>

<221> variation

<222> (11)...(11)

<223> N at position 11 is G ot T

<400> 181

aagtacagtg ngaggaacag cg

22

<210> 182

<211> 22

<212> DNA

<213> homo sapien

<220>

<221> variation

<222> (12)...(12)

<223> N at position 12 is A or G

<400> 182

attcctaataa antagaaatg ca

22

<210> 183

<211> 23

<212> DNA

<213> homo sapien

<400> 183

tttctgtttc aattcttgtc tat

23

<210> 184

<211> 23

<212> DNA

<213> homo sapien

<400> 184

tttctgtttc agttcttgtc tat

23

<210> 185

<211> 21

<212> DNA

<213> homo sapien

<400> 185

ggcccctgcc ttattattac t

21

<210> 186

<211> 21

<212> DNA

<213> homo sapien

<400> 186

ggcccctgcc gtattattac t

21

<210> 187
<211> 21
<212> DNA
<213> homo sapien

<400> 187
cactgtctgg gttttaatgt c

21

<210> 188
<211> 21
<212> DNA
<213> homo sapien

<400> 188
cactgtctgg cttttaatgt c

21

<210> 189
<211> 22
<212> DNA
<213> homo sapien

<220>
<221> variation
<222> (11)...(11)
<223> N at position 11 is A or G

<400> 189
tgagagaatt ncttgaaccc gg

22

<210> 190
<211> 21
<212> DNA
<213> homo sapien

<220>
<221> variation
<222> (11)...(11)
<223> N at position 11 is C or T

<400> 190
tttgctgaaa naatcactga c

21

<210> 191
<211> 22
<212> DNA
<213> homo sapien

<220>
<221> variation
<222> (11)...(11)
<223> N at position 11 is C or T

<400> 191
aacctcagtt ncctcatctg tg

22

<210> 192
<211> 21
<212> DNA
<213> homo sapien

<400> 192
aagaagtggc ttgtattttg c 21

<210> 193
<211> 21
<212> DNA
<213> homo sapien

<400> 193
aagaagtggc ctgtattttg c 21

<210> 194
<211> 23
<212> DNA
<213> homo sapien

<220>
<221> variation
<222> (11)...(11)
<223> N at position 11 is A or G.

<400> 194
aactgatttg nttggtatag ctg 23

<210> 195
<211> 20
<212> DNA
<213> homo sapien

<400> 195
aataaagata atttccttgg 20

<210> 196
<211> 20
<212> DNA
<213> homo sapien

<400> 196
aataaagata gtttccttgg 20

<210> 197
<211> 22
<212> DNA
<213> homo sapien

<400> 197
ttcctgcccc gacactcccg cc 22

<210> 198
<211> 22
<212> DNA
<213> homo sapien

<400> 198
ttcctgcccc cacactcccg cc

22

<210> 199
<211> 22
<212> DNA
<213> homo sapien

<220>
<221> variation
<222> (11)...(11)
<223> N at position 11 is A or G.

<400> 199
ttgggaggct naggcaggag aa

22

<210> 200
<211> 22
<212> DNA
<213> homo sapien

<400> 200
tgtcagctgt tactggaagt gg

22

<210> 201
<211> 22
<212> DNA
<213> homo sapien

<400> 201
tgtcagctgc tgctggaagt gg

22

<210> 202
<211> 21
<212> DNA
<213> homo sapien

<400> 202
aggagctggc cgaagccaca a

21

<210> 203
<211> 21
<212> DNA
<213> homo sapien

<400> 203
aggagctggc tgaagccaca a

21

<210> 204
<211> 21
<212> DNA
<213> homo sapien

<400> 204
aatgatgccca ccaaacaaat g 21

<210> 205
<211> 21
<212> DNA
<213> homo sapien

<400> 205
aatgatgccca tcaaacaaat g 21

<210> 206
<211> 21
<212> DNA
<213> homo sapien

<400> 206
gaggtggctc cgatgaccac a 21

<210> 207
<211> 21
<212> DNA
<213> homo sapien

<400> 207
gaggtggctc tgatgaccac a 21

<210> 208
<211> 21
<212> DNA
<213> homo sapien

<400> 208
ttccttaaca gaaatagtat c 21

<210> 209
<211> 21
<212> DNA
<213> homo sapien

<400> 209
ttccttaaca aaaatagtat c 21

<210> 210
<211> 21
<212> DNA
<213> homo sapien

<400> 210
ggaagtgttc caaaagagaa a 21

<210> 211
<211> 34
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic primer

<400> 211
gtatttttgc aaggctacca gttacatttg acaa 34

<210> 212
<211> 28
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic primer

<400> 212
gattggcttc aggatgtcca tgttggaa 28

<210> 213
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic primer

<400> 213
gctgctgtga tggggtatct 20

<210> 214
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic primer

<400> 214
acctcactca cacctgggaa 20

<210> 215
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic primer

<400> 215
caagtgagtg cttgggattg 20

<210> 216
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic primer

<400> 216
tgcttttatt cagggactcc a 21

<210> 217
<211> 25
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic primer

<400> 217
gtgatcccag cgtggtgttt gtctt 25

<210> 218
<211> 37
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic primer

<400> 218
gaaaggccag aggtactcac agcgaagatc ttgaggg 37

<210> 219
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic primer

<400> 219
tcgttttatt cagggactcc a 21

<210> 220
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic primer

<400> 220
caagtgagtg cttgggattg 20

<210> 221
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic primer

<400> 221
cccatgcact gcagagattc 20

<210> 222
<211> 21
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic primer

<400> 222
gcaaattcaa atttctccag g 21

<210> 223
<211> 35
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic primer

<400> 223
gagaagagcc accctgggtc caaccagaag aggat 35

<210> 224
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic primer

<400> 224
aaggcaggag acatcgctt 19

<210> 225
<211> 36
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic primer

<400> 225
gagcagttct gatgctggcc tgggcagcga ccacga 36

<210> 226
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic primer

<400> 226
tctgcacctc tcctoctctg 20

<210> 227
<211> 35
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic primer

<400> 227
cagcttggga agatttatga caggactgga cacga 35

<210> 228
<211> 18
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic primer

<400> 228
atgcccctgc caacttac 18

<210> 229
<211> 27
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic primer

<400> 229
gtgcaattac gttgtccctg ccacact 27

<210> 230
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic primer

<400> 230
ccatacagca aaagtagaag ggctagcaca 30

<210> 231
<211> 16
<212> DNA
<213> homo sapien

<220>
<221> variation
<222> (7)...(10)
<223> N at position 7-10 is A, T, C, or G

<400> 231
agatcannnn aggtca 16

<210> 232
<211> 16
<212> DNA
<213> Homo sapien

<400> 232
agatcacttg aggtca 16

<210> 233
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Primer

<400> 233
cagcgcttcc cgcgcgtctt ag 22

<210> 234
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Primer

<400> 234
ccactcactc tcgtccgcaa ttac 24

<210> 235
<211> 38
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Primer

<400> 235
ctgctgagtg actgaactac ataaacagag gccgggta 38

<210> 236
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Primer

<400> 236
ccactcactc tcgtccgcaa ttac 24

<210> 237
<211> 22
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Primer

<400> 237
cagcgcttcc cgcgcgtctt ag 22

<210> 238
<211> 24
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Primer

<400> 238
ccactcactc tcgtccgcaa ttac 24

<210> 239
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Primer

<400> 239
ctggctttct gctgagtgc 20

<210> 240
<211> 19
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Primer

<400> 240
gatcaaagtc cccgaaacc 19

<210> 241
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Primer

<400> 241
actcagttgt ataaccact gaaaatgagt 30

<210> 242
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Primer

<400> 242
ttctatagat gttatcatct ggg 23

<210> 243
<211> 30
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Primer

<400> 243
actcagttgt ataaccact gaaaatgagt 30

<210> 244
<211> 23
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Primer

<400> 244
ttctatagat gttatcatct ggg 23

<210> 245
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Primer

<400> 245
tcatactaagg cacgttgagg 20

<210> 246
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Primer

<400> 246
cctcaagcct ggagtgactt 20

<210> 247
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Primer

<400> 247
atggcaaaca gtccccaag 20

<210> 248
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Primer

<400> 248
accctagcgc tgtgtctctg 20

<210> 249
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Primer

<400> 249
atggcaaaca gtcctccaag 20

<210> 250
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Primer

<400> 250
accctagcgc tgtgtctctg 20

<210> 251
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Primer

<400> 251
tgtgtgtcct cccttccatt 20

<210> 252
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Primer

<400> 252
cttggaggac tgtttgccat 20

<210> 253
<211> 38
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Primer

<400> 253
cccctcctgc tttatctttc agttaatgac cagccccg 38

<210> 254
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Primer

<400> 254
atccccaact caaaaccaca

20

<210> 255
<211> 37
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Primer

<400> 255
gccgctgcct tccagggctc ccgagccaca cgctgcg

37

<210> 256
<211> 20
<212> DNA
<213> Artificial Sequence

<220>
<223> Synthetic Primer

<400> 256
atccccaact caaaaccaca

20